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PERNICIOUS ANAEMIA OF PREGNANCY AND THE PUERPERIUM

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Addisonian pernicious anaemia is an uncommon disease, but pernicious anaemia of pregnancy is much rarer still. Thus of 521 cases of macrocytic anaemia examined by us during the past seven years only 31 were associated with pregnancy and of these only four have been seen since the introduction of folic acid. It is therefore not surprising that no report on the therapeutic value of folic acid on this type of megaloblastic anaemia has appeared in British medical literature, and that records of only four cases have been published in America—three cases by Spies (1946) and one by Moore *et al.* (1945). In all four cases folic acid was given by the parenteral route, and a satisfactory response was obtained in each instance. We now submit records of three cases of pernicious anaemia of pregnancy and one case of Addisonian pernicious anaemia that relapsed as a result of pregnancy, all of which responded to folic acid. The haemoglobinometer used in this investigation was a Haldane instrument standardized by the National Physical Laboratory.

Case 1

A married woman aged 30 was admitted to our wards on Nov. 13, 1947, on account of severe anaemia. Her first confinement was in December, 1944, and the second in July, 1946. Because of anaemia she was treated in 1946 with iron before parturition and with anahaemin for three months subsequently and gradually made a good recovery. No details are available in regard to the type or the severity of the anaemia. In 1947 she again became pregnant and was confined in a neighbouring hospital on Nov. 2. Twins were delivered, and she lost a considerable amount of blood. No information about the state of her blood previous to this confinement was available other than the fact that her haemoglobin was 48% one month before delivery. During this month she was given 6 gr. (0.4 g.) of ferrous sulphate thrice daily and 2 ml. of anahaemin twice weekly. Consequent on the loss of blood at parturition the haemoglobin level fell to 40%.

After admission to our wards questioning revealed that her social and dietetic history was satisfactory and that there was no family history of anaemia or of diarrhoea. The patient had never been abroad and had never suffered from dyspepsia, dysphagia, or diarrhoea. Physical examination revealed no abnormality of the tongue, finger-nails, or skin. There was no subjective or objective evidence of involvement of the nervous system, and no source of blood loss was discovered. There was no jaundice or fever. The liver, spleen, and lymph nodes were not enlarged, and no pathological features were found in any system other than the haemopoietic system. A test meal revealed free hydrochloric acid in all specimens, and the urine contained an excess of urobilinogen. Her blood count on Nov. 14 was: red cells, 1,570,000 per c.mm.; haemoglobin, 30%; colour index, 0.96; reticulocytes, 1.4%; white cells, 12,400 per c.mm. A megaloblastic bone marrow indistinguishable from that of Addisonian pernicious anaemia was found. Folic acid was given in a dosage of 20 mg. daily by mouth for 12 days, and thereafter 10 mg. daily. This resulted in a reticulocyte peak of 31% on the fifth day and an increase of red cells and haemoglobin of 2,400,000 and 58% respectively in 55 days. (Fig. 1.)

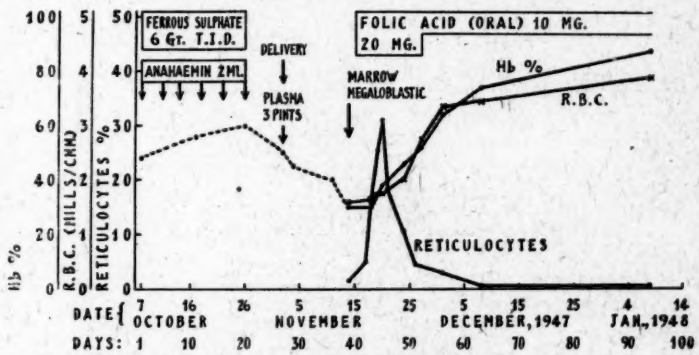
FERROUS SULPHATE 6 GR. T.I.D.
ANAHAEMIN 2ML.
DELIVERY
PLASMA 3 PINTS
FOLIC ACID (ORAL) 10 MG. 20 MG.
MARROW MEGALOBLASTIC
Hb %
R.B.C.
RETICULOCYTES
Hb %
R.B.C. (MILLS/CMM.)
RETICULOCYTES %
DATE { 7 16 26 5 15 25 5 15 25 4 14
OCTOBER NOVEMBER DECEMBER, 1947 JAN., 1948
DAYS: 1 10 20 30 40 50 60 70 80 90 100

FIG. 1.—Chart of Case 1. ----- indicates counts done before we saw the patient.

Case 2

This patient, a married woman aged 23, was admitted to the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, on Jan. 29, 1948, with a diagnosis of pre-eclamptic toxaemia because of oedema, albuminuria, and hypertension. On Feb. 7 she was delivered of a healthy full-time female child. There was no history of previous pregnancy or of miscarriages. A haemoglobin level of 60% was found the day before the baby was born.

The patient said she had always been pale, but the only serious illness she had had was diphtheria at the age of six, which was followed by a right-sided hemiplegia. There was no family history of anaemia or diarrhoea. She was pale and slightly built, had never suffered from dysphagia, dyspepsia, or diarrhoea, and had never been abroad. Her dietetic history was satisfactory. There was no enlargement of the liver, spleen, or lymph nodes. The tongue was slightly atrophic, with several

sore patches, and the finger-nails showed some ridging. There was no jaundice, and no source of blood loss was discovered. The urine contained albumin and a marked excess of urobilinogen. A test meal showed histamine-fast achlorhydria. The blood pressure was normal, and no disease was found in the cardiovascular or respiratory system. Apart from the residual signs of the hemiplegia mentioned above no abnormality of the nervous system was found.

A blood count carried out by us on Feb. 20 was as follows: red cells, 2,300,000 per c.mm.; haemoglobin, 44%; colour index, 0.9; white cells, 4,000; reticulocytes, 1.2%. The bone marrow was megaloblastic and indistinguishable from that of untreated Addisonian pernicious anaemia, despite the fact that 2 ml. of anahaemin had been given on three consecutive days before sternal biopsy was undertaken. Eight days later the blood count was slightly lower and the M.C.V. was 84 c.μ. The state of the bone marrow could not be ascertained, since the patient refused to have a second sternal puncture. The presence of an occasional megaloblast in the peripheral blood suggested that no change had occurred. Accordingly treatment with folic acid was started, a single injection of 30 mg. being given intramuscularly, followed by 10 mg. by mouth daily. This resulted in a reticulocyte peak of 26% on the fifth day, and an increase of 1,380,000 red cells and 12% haemoglobin in 18 days. At this date the colour index was 0.75, and the hypochromic appearance of the erythrocytes clearly indicated the need for supplementary iron therapy.

Case 3

A married woman aged 30 was transferred to our wards from the Simpson Memorial Maternity Pavilion on Feb. 26, 1947, on account of severe anaemia. She had given birth to a healthy son on Feb. 14 and had had no previous pregnancies. Labour had been uneventful except that there had been a moderately heavy blood loss after delivery of the placenta. There was no family history of anaemia or diarrhoea. Her appetite was good. The patient's dietetic history was satisfactory and she had never suffered from dysphagia, dyspepsia, diarrhoea, anaemia, or any serious illness. Physical examination revealed no abnormality of the heart, lungs, abdominal organs, or nervous system. There was some atrophy of the papillae of the tongue; neither koilonychia nor enlargement of lymphatic nodes was found. The blood pressure was 124/90. The urine contained a trace of albumin but no excess of urobilinogen. There was free hydrochloric acid in the gastric juice.

When we first saw the patient on Feb. 26 the blood count was: red cells, 1,800,000 per c.mm.; haemoglobin, 46%; colour index, 1.28; white cells, 6,800 per c.mm.; reticulocytes, 5.6%. The M.C.V. calculated on two occasions was 107 and 114 c.μ. The marrow was megaloblastic. The patient had been treated with 6 gr. (0.4 g.) of ferrous sulphate three times a day during pregnancy, but had never received liver by mouth or by injection. At the end of a control period of ten days the red cell count was unaltered and the reticulocyte count had fallen to 1.8%. Accordingly, 10 mg. of folic acid daily was given by mouth. She had to leave hospital on account of domestic difficulties, but continued to take the folic acid as an outpatient, reporting at regular intervals to the blood clinic for assessment of progress. A rapid improvement in her general clinical condition resulted, while a gain of 1,410,000 red cells and 10% haemoglobin occurred in 35 days. She was then given 18 gr. (1.2 g.) of ferrous sulphate daily and the blood count was restored to normal.

Case 4

This patient, an unmarried woman aged 38, was in the sixth month of pregnancy when we were asked to see her because of severe anaemia which had failed to respond to treatment with iron and various preparations of liver.

In 1940, at the age of 30, she had been admitted to the Royal Infirmary of Edinburgh suffering from severe anaemia. The following information was obtained from her case records. Before admission she had been getting increasingly pale, easily tired, and breathless, and vomiting and diarrhoea had occurred. There was oedema of the ankles, the skin had a lemon-yellow colour, and the conjunctival mucous membrane was very pale. Apart from atrophic glossitis, anaemia, and achlorhydria, no abnormality was noted in any system. Her blood count on April 15, 1940, was: red cells, 1,720,000 per c.mm.; haemoglobin, 45%; colour index, 1.3. Intensive treatment with parenteral liver extract was given. She received an intramuscular injection of 5 ml. of "pernaemon" daily. As the response was poor, "campolon," one ampoule daily, was substituted. The response continued to be poor, and despite this intensive treatment the gain in red cells and haemoglobin over a period of two and a half months was only 1,500,000 red cells and 25% haemoglobin. After discharge from hospital the patient continued to have injections of liver extract from her doctor, at first daily and then weekly for the next two years.

FIG. 2.—Bone marrow from Case 4, showing persistence of megaloblastic erythropoiesis despite administration of 32 ml. anahaemin, 6 ml. plexan, and 3¼ oz. (115 g.) of hepamino over a period of 3 weeks. (×1,400.)

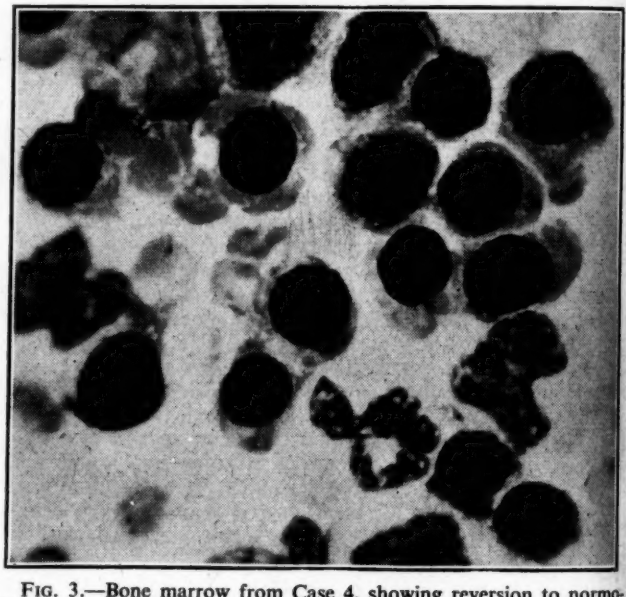

FIG. 3.—Bone marrow from Case 4, showing reversion to normoblastic erythropoiesis 36 hours after the intramuscular administration of 60 mg. of folic acid. (×1,400.)

In 1942 she had two severe reactions following the injection of liver extract. When anahaemin was substituted for the previous liver extract no reactions followed. The doctor states, however, that the patient attended for treatment irregularly and at long intervals during the next five years. Throughout this period she was pale, breathless, and easily tired, but continued working

most of the time. In July, 1947, she reported to her doctor because she was pregnant, and was admitted to the Royal Infirmary on Dec. 22, 1947, because of severe anaemia.

The patient was extremely pale but showed no obvious loss of weight. She stated that her appetite was poor and that she frequently suffered from flatulent dyspepsia and had occasional attacks of diarrhoea. A dietary history indicated that her intake of animal protein and vitamin C in particular was very unsatisfactory. Glossitis and koilonychia were absent. There was no enlargement of liver, spleen, or lymph nodes. A test meal revealed histamine-fast achlorhydria. During her stay in hospital she had no diarrhoea. In view of her irregular and insufficient treatment with liver extract, particular attention was paid to examination of the nervous system. Although she stated that she had never had any paraesthesiae or ataxia, indubitable signs of involvement of the spinal cord were found—namely, grossly exaggerated reflexes in both lower limbs and a bilateral extensor plantar response. Apart from a mild degree of incoordination no evidence was obtained of involvement of the peripheral nerves or posterior columns of the cord.

Her blood count was : red cells, 1,200,000 per c.mm. ; haemoglobin, 28% ; white cells, 3,600 ; the M.C.V. on two occasions was 93.9 c.μ and 92.7 c.μ ; the blood picture was typical of pernicious anaemia, and her bone marrow was megaloblastic. In view of her grave clinical state she was given

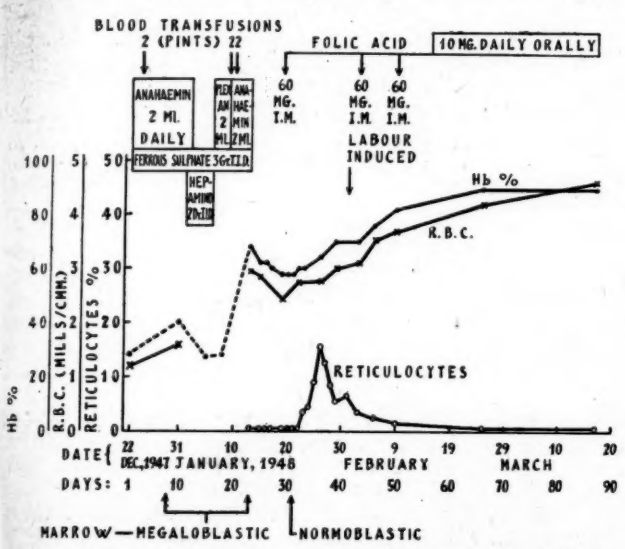

FIG. 4.—Chart of Case 4. ------ indicates counts done before we saw the patient.

a transfusion of blood. During the next 14 days she received 3 gr. (0.2 g.) of ferrous sulphate three times a day, and 32 ml. of anahaemin, 6 ml. of "plexan," and 3½ oz. (115 g.) of proteolysed liver ("hepamino"). As no clinical or haematological improvement resulted a further transfusion of 4 pints (2.3 litres) of blood was given, and this raised her red cell and haemoglobin levels to 2,980,000 per c.mm. and 68% respectively. A second sternal puncture indicated that the marrow was still megaloblastic (Fig. 2). After a control period of six days, during which no therapy was given, the red cells had fallen to 2,480,000 per c.mm. and the haemoglobin to 58%. The reticulocyte count never exceeded 1%.

Accordingly, treatment with folic acid was started, a single injection of 60 mg. being given intramuscularly. A third sternal puncture carried out 36 hours later showed a remarkable transformation of the marrow to the normoblastic state (Fig. 3). This was followed by a rise in the reticulocyte count, the peak of 15.6% occurring on the eighth day, and a dramatic improvement in the patient's clinical condition. A gain of 600,000 red cells and 12% haemoglobin occurred in ten days. On the fourteenth day after the first injection of folic acid labour was induced. A second injection of 60 mg. of folic acid was given next day, and a third injection of the same quantity seven days later. Thereafter she received 10 mg. daily by mouth, and on the 59th day after the initial injection of folic acid her red cells amounted to 4,630,000 and haemoglobin to 90% (Fig. 4).

It is of interest to note that the patient's father had suffered from pernicious anaemia for nine years, and that there was a remarkable history of the premature development of white hair on the paternal side of the family. We have previously noted in other patients who have developed pernicious anaemia at a surprisingly early age that a family history of the disease is commonly obtained.

Discussion

The first large series of cases of pernicious anaemia of pregnancy in Great Britain was recorded by Stevenson (1938). As this investigation was carried out before sternal puncture became a routine haematological procedure it is possible that certain of the cases might not have fulfilled the essential criterion of having a megaloblastic bone marrow. The literature dealing with pernicious anaemia of pregnancy has been fully reviewed by Callender (1944), who described 25 cases which she observed personally. In 1942 Davidson, Davis, and Innes described 16 cases, and Davidson and Davis (1947) drew attention to four points of particular importance. (1) The diagnosis of pernicious anaemia of pregnancy depends essentially on the demonstration of typical megaloblasts in the bone marrow, since the peripheral blood picture may be quite unlike that of Addisonian pernicious anaemia, the colour index may be below unity, and the M.C.V. within normal limits. (2) Although free hydrochloric acid is often present in the gastric juice, in a number of cases a histamine-fast achlorhydria is found. In such cases it may be difficult or impossible to decide whether the case should be classified as pernicious anaemia of pregnancy or Addisonian pernicious anaemia complicated by pregnancy unless the effect of stopping all forms of liver therapy is observed for a period lasting up to two years. (3) The response to parenteral liver therapy may be normal, poor and delayed, or absent. (4) Cases refractory to parenteral liver therapy will respond promptly to oral treatment with proteolysed liver (hepamino) or to cooked liver (Fullerton, 1943).

It will be noted that Cases 1, 3, and 4 all failed to respond to the parenteral injection of large amounts of well-known liver extracts of various types, both crude and refined, but responded promptly to folic acid given either parenterally or orally. No liver therapy was given to Case 3 prior to the administration of folic acid. Case 4 failed to respond to proteolysed liver, but the quantity given was inadequate and the period of treatment (5 days) too short for the attainment of a successful therapeutic effect.

No satisfactory explanation is as yet available of the mechanism underlying the development of a megaloblastic anaemia in pregnant women. The anaemia could develop as a result of defective intake of some factor necessary for normal blood formation, from a failure in the production of Castle's intrinsic factor, or from a defect in absorption from the alimentary tract. We were particularly interested in the possibility of malabsorption because of our past experience of a case diagnosed as pernicious anaemia of pregnancy and two cases diagnosed as idiopathic refractory megaloblastic anaemia which were subsequently shown to be cases of idiopathic steatorrhoea, although diarrhoea was absent in all three patients throughout the period of investigation in hospital (Davidson, 1948). Although none of the patients in this series had diarrhoea or fatty stools during their stay in hospital, a fat-balance test was carried out in Cases 1 and 4. The results showed no evidence of defective malabsorption of fat. We realize, of course, that this finding does not rule out the possibility of a selective malabsorption of other factors required for the continuation of normoblastic blood formation.

Folic acid would seem to be the best agent available at the present time for the treatment of pernicious anaemia of pregnancy because it can be administered orally in the

form of a small tasteless tablet and because of the rapid clinical and haematological improvement which results even in cases refractory to parenteral liver therapy. Since the duration of treatment with folic acid is limited to a few weeks, the danger of producing subacute combined degeneration of the cord is greatly reduced as compared with Addisonian pernicious anaemia. Further time must elapse, however, before it can be stated confidently that neurological features will not occur in patients with pernicious anaemia of pregnancy receiving folic acid.

As many cases of pernicious anaemia of pregnancy are suffering from a dual deficiency of iron and the factor required for maintenance of normoblastic blood formation it is desirable that both deficiencies be corrected simultaneously. While our patients were receiving folic acid iron was deliberately withheld in order to simplify the interpretation of the therapeutic response.

(Anahaemin is a refined liver extract, and "plexan" and "campolon" are crude extracts.)

Summary

Three cases of pernicious anaemia of pregnancy and one case of Addisonian pernicious anaemia complicated by pregnancy responded excellently to treatment with folic acid. Three of the cases had failed to respond to the parenteral injection of liver extracts prior to the administration of folic acid.

We wish to thank Prof. Kellar, Dr. Fahmy, and others of our colleagues in the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, for permission to investigate and treat the above cases.

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FOLIC ACID*

BY

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Idiopathic Steatorrhoea and Coeliac Disease

A number of reports have now appeared on the excellent effect of "folic acid" in the treatment of tropical sprue (Darby and Jones, 1945; Darby *et al.*, 1946a, 1946b; Spies, 1946a, 1946b; Spies *et al.*, 1946; Manson-Bahr and Clarke, 1946; Morrison and Johnston, 1947); while Davidson and Girdwood (1947) and Weir and Comfort (1947) have described their results using it on patients with non-tropical sprue, particularly those with normoblastic marrows.

*The conclusion of the lectures (abridged) given to the Section of Experimental Medicine of the Royal Society of Medicine on May 13, 1947, and to the Medical Society of London on Feb. 9, 1948.

The following four cases illustrate my results when pteroylglutamic acid is used on patients with idiopathic steatorrhoea (non-tropical sprue) and coeliac disease (Table V).

Idiopathic Steatorrhoea

The diagnostic criteria for patients with idiopathic steatorrhoea (non-tropical sprue) were: (1) a macrocytic anaemia with a megaloblastic or normoblastic marrow; (2) frequent loose, bulky, offensive stools, often yellowish in colour; (3) high total fat content of stools with or without a prior fat test meal; (4) achlorhydria gastrica or normal acidity; (5) soreness or ulceration of the mouth or tongue; (6) severe loss of weight; and (7) a flat glucose-tolerance curve.

Case I.S.—A housewife aged 53 had an eight-months history of tiredness, lack of energy, palpitation, intermittent soreness of the tongue, increasing pallor, and frequent loose, bulky, offensive, yellowish stools up to eight in 24 hours. She had lost at least 3 st. (19 kg.) in weight. The bone marrow was very cellular and active, with a mixed megaloblastic (5%)–normoblastic (27%) hyperplasia. A blood count showed: R.B.C., 2,610,000; Hb, 72%; C.I., 1.33; W.B.C., 6,600 (polymorphs, 73%, lymphocytes 22%, large monocytes 3%, eosinophils 2%); marked anisocytosis and poikilocytosis; reticulocytes, 3.2%. Stools: total fat, 55% (split fat 83%, unsplit 17%). She was given 20 mg. of pteroylglutamic acid orally per day. There was slight reticulocytosis (4.2% on the 8th day) and the haematological response was slow but ultimately (after 64 days) reached R.B.C. 4,140,000, Hb 82%, C.I. 1, W.B.C. 7,100, with a normal differential white cell count. The stools rapidly improved, became formed, and ceased to be frequent, bulky, or offensive; total fat, 28% (split 84%, unsplit 16%). Clinically the patient had improved very much indeed; she was free from symptoms and was gaining weight steadily when discharged from hospital.

Case B.C.—A housewife aged 35 had had tetany intermittently since the age of 24; she had bilateral cataracts and frequent bulky offensive stools in addition to the usual general symptoms. Examination revealed achylia gastrica, a flat glucose-tolerance curve, a negative Wassermann reaction, and normal C.S.F.; serum calcium varied between 6.4 and 9.8 mg. per 100 ml., blood urea 22 mg. per 100 ml., urea clearance 85%, serum phosphorus 3.6%, plasma alkaline phosphatase 4–14 units; radiologically there was some generalized osteoporosis of the long bones; weight, 4 st. 12 lb. (30.84 kg.); blood pressure, 100/70. A blood count on June 27, 1946, showed: R.B.C., 3,210,000; Hb, 74%; C.I., 1.16; W.B.C., 3,600 (polymorphs 59%, lymphocytes 36%, large monocytes 4%, eosinophils 1%); anisocytosis and poikilocytosis marked; platelets 97,000. The marrow was very active and cellular and showed a mixed megaloblastic (4.7%)–normoblastic (9.7%) reaction. Stools: total fat, 41% (split fat 82%, unsplit fat 18%). Bacteriological examination of faeces did not disclose any abnormality.

The patient had 15 mg. of pteroylglutamic acid intramuscularly daily for 10 days without any clinical or haematological response, and was then given 1 oz. (28 g.) orally of proteolysed liver extract daily without improvement, the blood count on Aug. 9 being rather worse: R.B.C., 2,820,000; Hb, 62%; C.I., 1.11; W.B.C., 7,200. At this stage the sternal marrow showed a normoblastic (49.25%) hyperplasia. Continued treatment with liver extract parenterally, supplementary synthetic vitamins of the B complex, hog's stomach, etc.,

TABLE V.—*Idiopathic Steatorrhoea*

Case	Sex	Age	Marrow	Gastric Acidity	R.B.C. × 10^6	Hb %	W.B.C.	Folic Acid
I.S.	F	53	Mbl 5% Nbl 27%	Achylia	2·61 4·14 (69)	72 82 (69)	6,600 7,100	20 mg. orally
B.C.	F	35	Mbl 4·7% Nbl 9·7% Mbl 0 Nbl 49·25%	Achylia	3·21 3·11 (14) 3·49 4·31 (32) 2·80 (187) 3·08 (201)	74 72 (14) 70 84 (32) 74 (187) 64 (201)	3,600 5,200 (14) 9,700 7,400 (32) 9,000 (187) 12,800 (201)	15 mg. [10] i.m. 50 mg. [2] i.v. 50 mg. [25] i.v. 40 mg. [187] orally
H.C.	F	27	Mbl 10·4% Nbl 10·4%	Normal	1·97 5·35 (107)	50 108 (107)	3,200 5,700	20 mg. [107] orally
J.M.	F	3	Mbl 2·25% Nbl 2·5%	Normal	3·12 3·81 (129)	63 44 (129)	4,500 4,300 (129)	5 mg. [129] orally

Reticulocytes: Case I.S. 4·3% (8); Case H.C. 25·4% (7). Nbl = Normoblasts. Mbl = Megaloblasts. ( )Day after beginning treatment. [ ] No. of days on treatment

duced a slightly better response, with a rise on Sept. 13 to R.B.C. 3,490,000 and Hb 70%. She was again given 50 mg. of pteroylglutamic acid intravenously on two successive days, and although there was no reticulocyte response the count rose to R.B.C. 4,310,000 and Hb 84% on Oct. 11. A further 50 mg. was given intravenously, and she was transferred to the convalescent home distinctly better with almost normally formed stools. After return home the pteroylglutamic acid was discontinued and she gradually relapsed; the bowels again became loose and the stools fluid, offensive, and yellow; she lost weight (4 st. 9 lb.—29.48 kg.); serum calcium was 8.5 mg. per 100 ml.; and on April 23, 1947, the blood count was: R.B.C., 2,800,000; Hb, 74%; C.I., 1.3; W.B.C., 9,000. The sternal marrow was still normoblastic.

Pteroylglutamic acid was recommenced at 40 mg. orally per day, but this apparently made the stools worse again and they remained very troublesome. The blood count rose very slowly, and on Sept. 10 it was R.B.C., 4,180,000; Hb, 80%; W.B.C., 11,900. She was put on to proteolysed liver, "sprulac," calcium gluconate, and calciferol, the blood count reaching: R.B.C. 4,400,000, Hb 84%, W.B.C. 11,200 on Oct. 8.

Case H.C.—A housewife, then aged 20, was first seen in 1940 with a refractory macrocytic anaemia for which various treatments and frequent blood transfusions at intervals of two to three weeks were tried with moderate to poor results. In 1945 she attended my clinic complaining of some intermittent diarrhoea which cleared up with treatment, but in January, 1946, it had become very troublesome and less responsive to treatment. In April, 1946, for the first time the stools were bulky, greasy, and soft, contained total fat 74% (split fat 75%, unsplit fat 25%), while the occult blood reaction was negative. There was a normal gastric acidity. *X*-ray examination showed general osteoporosis of skull, pelvis, and long bones, and bilateral fractures of the ischio-pubic junctions. She was treated with high supplementary vitamins, calcium, oral liver extract, etc., and some clinical improvement was obtained, but the blood count reached R.B.C. 3,840,000, Hb 92%, W.B.C. 5,000 on only one occasion; *x*-ray examination of the skeleton revealed marked improvement in the osteoporosis, which had nearly gone. Thereafter she relapsed again and on Nov. 15, 1946, had a count of R.B.C. 1,970,000, Hb 50%, C.I. 1.25, W.B.C. 3,200.

She was given pteroylglutamic acid (20 mg. orally per day), with a very good haematological response—reticulocytes 25.4% on the 7th day—while the count rose steadily on 10 mg. daily to R.B.C. 5,350,000, Hb 108%, C.I. 0.99 on March 12, 1947; radiologically the skeleton did not show any osteoporosis. She became pregnant but aborted in October, 1947 (R.B.C. 4,810,000, Hb 98%). She remained quite well until Jan. 19, 1948, when the blood had relapsed to R.B.C. 2,940,000, Hb 70%, W.B.C. 3,400, and she complained of a recurrence of the old symptoms; the bone marrow was of an active mixed megaloblastic-normoblastic type.

Coeliac Disease

Case J.M.—A girl aged 3 (under care of Dr. M. Egan) was diagnosed as having coeliac disease, with enlarged abdomen, general wasting (weight 1 st. 7 lb.—9.53 kg.), frequent bulky foul stools—total fat 45.6% (split fat 88%, unsplit fat 12%). The spleen, liver, and glands were not enlarged; the nervous system and gastric acidity were normal. The glucose-tolerance curve was: 100, 110, 110, 100—no glycosuria. The sternal marrow contained 2.25% megaloblasts and 2.5% normoblasts. A blood count showed: R.B.C., 3,120,000; Hb, 63% (8.7 g.); C.I., 1.10; W.B.C., 4,500. She was given 5 mg. of pteroylglutamic acid daily for 19 weeks, which was supplemented with ferric ammonium citrate or ferrous sulphate and vitamin C (50 mg. daily) without any haematological improvement; at the end of that time the blood count was: R.B.C., 3,810,000; Hb, 44%; C.I., 0.5; W.B.C., 4,300. Nevertheless, although there was some slight improvement in the stools, which before discharge from hospital had become more formed, she had recurrences of the frequent bulky offensive stools.

The response in this case was disappointing and contrasts with the two cases described by Dalton, Thomson, and Wilson (1946)—both of which had megaloblastic marrows and responded well—and the case of Brody and Gore (1946). On the other hand, Davidson and Girdwood's cases had normoblastic marrows and did not do well, while six of Tegelaers and Weyers's (1947) children improved clinically without haematological improvement.

Of my three patients with steatorrhoea, Cases I.S. and H.C. did very well, showing steady improvement after folic acid, with relief of symptoms and the intestinal steatorrhoea. Case H.C. was particularly good, and early osteoporosis in the skeleton also cleared up, but the patient relapsed later. Case B.C. was less satisfactory, but did ultimately show marked improvement, although relapsing later when the pteroylglutamic acid was discontinued and failing to give much response to a second course.

The cases of non-tropical sprue of Darby *et al.* (1946a, 1946b) also showed good responses, but in the seven cases of Weir and Comfort (1947), and nine out of 10 cases of steatorrhoea and sprue described by Davidson and Girdwood (1947), the haematological responses were unsatisfactory: macrocytosis persisted, yet there was clinical improvement, and the diarrhoea was better although fat absorption was still abnormal. The excellent claims for folic acid in the treatment of sprue by Spies and collaborators and other American authors would appear to require further explanation, and it is probable that their cases were suffering from severe nutritional deficiencies as well—a complication not often seen in this country.

Chronic Ulcerative Colitis

Following the variable results in coeliac disease, the good results claimed by Carruthers (1946) in the treatment of six patients with severe recurrent diarrhoea with folic acid lead naturally to a consideration of other intestinal disturbances. A patient with severe chronic ulcerative colitis of long standing failed to show the slightest evidence of relief when given 20–50 mg. of folic acid daily for three weeks, the blood count falling further and the colitis continuing without remission. Similar results have been obtained by others (Davidson and Girdwood, 1947).

Aplastic Anaemia, Agranulocytosis, Neutropenia, and Thrombocytopenia

One of the earliest observations (Endicott, Daft, and Ott, 1945) on folic acid was its importance in preventing or rapidly curing the marrow hypoplasia or aplasia produced in rats fed on folic-acid-free diets or given diets containing 1% sulphasuxidine, which inhibits the synthesis of folic acid by intestinal bacteria. This raised hopes that folic acid might also be of value in relieving the aplastic or hypoplastic conditions of the human marrow as seen in aplastic anaemia, agranulocytosis, chronic neutropenia, and thrombocytopenia.

In my experience and that of others (Doan, 1946, 6 hypoplastic patients; Goldsmith, 1946, 2 aplastic cases; Kaufmann and Schwager, 1946, 1 aplastic case; Peat and Branch, 1946, 1 aplastic case; Spies, 1946a, 1946b, 3 aplastic patients; Watson *et al.*, 1945, [redacted] refractory aplastic anaemias, 1 neutropenia; Zuelzer, 1946, 3 aplastic or hypoplastic children) the treatment of aplastic or hypoplastic anaemias with natural or synthetic folic acid has been most disappointing. Gendel (1947), however, has recently claimed to have had some slight responses in three cases of "aplastic" anaemia treated with enormous doses (400–500 mg. daily) of synthetic pteroylglutamic acid for long periods of time, with a reduction in the need for blood transfusions. His results were not very convincing, and one of his patients had a normoblastic marrow.

In my experience similar large doses have not produced any obvious effects. Pteroylglutamic acid in lesser doses

TABLE VI.—*Aplastic Anaemia*

Case	Sex	Age	Marrow	R.B.C. × 10^6	Hb %	W.B.C.	Platelets	Folic Acid Dosage
J.S.	M	44	Aplastic	1·52	30	4,200	40,000	150 mg. i.v.
				1·60 (7)	30 (7)	2,700 (7)	25,000 (9)	
P.S.	M	6	,,	1·37	18	1,800	35,000	5–100 mg. orally daily
				0·85 (56)	20 (56)	1,400 (56)	246,000 (56)	
				1·08 (308)	24 (308)	1,800 (308)		
M.L.	F	53	,,	1·38	26	3,800	30,000	100 mg. i.v.
								20 mg. orally daily

was given to three patients with typical aplastic anaemia (see Table VI): all had aplastic marrows and all failed to show the slightest clinical or haematological responses after doses varying up to 150 mg. a day intravenously and orally. Similar negative results were noted in patients with agranulocytosis and the cases of chronic neutropenia given up to 150 mg. daily, intravenously or orally, in contradistinction to the changes noted in rats (see above), while thrombocytopenia purpura (two cases secondary to gold therapy) also resisted this treatment.

Of course, as shown above, where there is haematological response to treatment, as in pernicious anaemia and similar megalocytic anaemias, all the cellular elements of the blood benefit, so that with the red cells there is concomitant improvement in the numbers of white cells and platelets, as occurs after liver and stomach therapy.

Leukaemias

A large number of cases of acute and chronic leukaemia were given synthetic pteroylglutamic acid without benefit. Thus patients with acute myeloblastic, lymphoblastic, and monocytic leukaemias who received up to 150 mg. intravenously and 20–80 mg. orally daily did not show improvement in their haematological or in their general clinical conditions. In chronic myeloid and lymphatic leukaemias no better results were seen, but two of my old patients with pernicious anaemia who developed chronic myeloid leukaemia showed marked general improvement in the pernicious anaemia but subsequently failed to maintain it.

Patient E.O., a woman aged 40, was first seen by me in 1932, when pernicious anaemia was diagnosed: her case has been reported by my chief assistant, Dr. Woolley (1944). She remained well until 1942 when, after five years' absence, she was found to have a large spleen—6 in. (15 cm.) below the costal margin—due to a chronic myeloid leukaemia, with R.B.C., 2,680,000; Hb., 48%; C.I., 0.92; W.B.C., 85,600 (polymorphs 59.8%, lymphocytes 7.2%, large monocytes 0.4%, eosinophils 2.4%, basophils 6.6%, metamyelocytes 14%, myelocytes 9%, myeloblasts 0.6%); normoblasts 6 in 500, megaloblasts 8 in 500 white cells. The sternal marrow puncture showed a chronic myeloid leukaemia picture with also normoblasts 6.6% and megaloblasts 6.6%. She did quite well on anti-pernicious-anaemia treatment with liver extract and additional *x*-ray therapy, and later urethane (1–3 g. daily), but on Feb. 13, 1947, the blood count had become worse, with R.B.C., 3,720,000; Hb, 74%; C.I., 1; W.B.C., 120,500. No improvement was shown haematologically on 20–40 mg. of pteroylglutamic acid daily.

Patient G.G., a woman aged 52, was originally seen in 1940 with pernicious anaemia which responded normally to routine treatment for four years, but on Oct. 16, 1945, she returned to my clinic with a spleen 2 in. (5 cm.) below the costal margin and a blood count of R.B.C., 3,610,000; Hb, 82%; C.I., 1.12; W.B.C., 82,600 (polymorphs 54.5%, lymphocytes 9.5%, large monocytes 4.5%, eosinophils 1.5%, basophils 4.5%, myelocytes 15.5%, metamyelocytes 3.5%, myeloblasts 6.5%); nucleated red cells, 4 in 200 white cells. Marrow biopsy showed a typical chronic myeloid leukaemia with no megaloblasts to be seen. The patient responded very well to liver extract and urethane, but after severe haematuria she had (Feb. 15, 1947) R.B.C., 1,710,000; Hb, 34%; C.I., 1; W.B.C., 219,500; and a typical myeloid leukaemia marrow with very few megaloblasts and normoblasts. She was given pteroylglutamic acid, 30 mg. daily orally, with improvement to April 9 (R.B.C., 3,260,000; Hb, 64%; C.I., 0.98), without any further increase subsequently. The white cell count fell to 7,900 (polymorphs 53%, lymphocytes 5.5%, monocytes 2%, eosinophils 1.5%, basophils 3%, myelocytes 24%, metamyelocytes 10%, myeloblasts 1%) following a course of tri-β-chlorethylamine hydrochloride.

Two patients with leuco-erythroblastic anaemia did not show any clinical or haematological response to synthetic pteroylglutamic acid in daily doses of 20–30 mg. orally for periods up to 38 days.

Miscellaneous Blood Diseases

Synthetic pteroylglutamic acid has also failed to initiate any clinical or haematological improvement in many other blood conditions not having megaloblastic marrow hyperplasia, such as acute and chronic haemolytic anaemias, microcytic hypochromic anaemias, anaemias secondary to hyperthyroidism and myxoedema, toxic anaemias, etc.

Recently Farber *et al.* (1947) reported their preliminary and somewhat favourable results in the treatment of 100 cases of malignant disease with two synthetic polyglutamates—pteroyldiglutamic acid ("diopterin") and pteroyltriglutamic acid ("teropterin"). Apparently pteroylglutamic acid was without effect, and these observers say that there is no evidence to indicate that those substances should be used in routine therapy.

Discussion

Evidence has been accumulating as to the value of this new synthetic anti-macrocytic-anaemia constituent of the vitamin B complex. It is quite clear that in general only those anaemias with megaloblastic marrows respond to pteroylglutamic acid, however administered, while those with normoblastic, aplastic, or hypoplastic marrows do not.

Thus of the megaloblastic anaemias that respond we have pernicious anaemia, possibly achrestic anaemia, and macrocytic anaemias of pellagra, sprue, idiopathic steatorrhoea, pregnancy, infancy, and nutritional deficiencies. In the sprue syndrome, coeliac disease and steatorrhoea may vary in response according to the type of marrow activity: with a megaloblastic marrow the response may be good for a time, but these patients tend to relapse with recurrence of the loose, bulky, fatty stool. Less satisfactory results are obtained when the marrow is normoblastic, and although these patients do not respond haematologically they may show some improvement in their intestinal functions. This has led Davidson and Girdwood to suggest that pteroylglutamic acid has two functions: to maintain normoblastic marrow action, and to control the behaviour of the alimentary tract.

The great difference between the sprue cases of American authors and those described in this country does suggest that the American patients may have had more gross nutritional deficiencies with superimposed gastro-intestinal disturbances, while the British ones are primarily due to a failure of absorption from the intestinal tract or else failure to utilize essential nutritional factors—in particular, members of the vitamin B group.

Among the various haematological conditions not responding to pteroylglutamic acid I have noted hypochromic microcytic and secondary anaemias, aplastic and hypoplastic types of anaemia, many "liver-refractory" anaemias, haemolytic anaemias, acute and chronic leukaemias, idiopathic and toxic thrombocytopenic purpura, agranulocytosis, chronic and toxic leucopenias.

However administered, the immediate effects of pteroylglutamic acid on patients with pernicious anaemia are good, although not quite so striking as may follow highly potent liver extracts or hog's stomach preparations. A good reticulocyte crisis is obtained in most but not all cases at about the seventh to ninth day, with conversion of the megaloblastic marrow reaction to a normoblastic one and a steady rise in the haemoglobin percentage and the red cell, white cell, and platelet values. Clinically, the patient begins to feel very much better; appetite and colour return, weight increases, gastro-intestinal symptoms improve, but there is a tendency for macrocytosis to remain, and the symptoms of peripheral polyneuritis or postero-lateral sclerosis either persist unchanged or become worse.

After only a few months eight of 20 patients with pernicious anaemia have neurological symptoms and signs—four coming on acutely in the course of one to three months after discharge from hospital. Similar disappointing results are now being obtained by others, and it is therefore very important that all patients with pernicious anaemia on pteroylglutamic acid should be kept under very frequent and constant haematological and clinical observation. Maintenance doses must not be reduced too much (5–15 mg. daily are commonly required), otherwise the haematological condition deteriorates and macrocytosis becomes more pronounced, with an even greater tendency to produce neurological changes.

Thus, while we recognize that pteroylglutamic acid has a very great and prompt haematological influence, in particular with the macrocytic megaloblastic anaemias, nevertheless we are compelled to take note of the very disquieting and disappointing fact that it has no influence at all in curing, relieving, or preventing the onset or progression of neurological symptoms and signs. There are now records of neurological changes developing or getting worse in 59 out of 184 patients treated. In fact, I have been particularly struck by the acuteness of the onset of signs and symptoms of subacute combined degeneration of the cord with changes in the reflex reactions that may come on within one to four months or so of the institution of pteroylglutamic acid therapy.

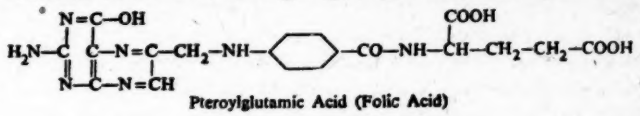
It is quite clear that pteroylglutamic acid has definite limitations and alone is not a safe treatment for pernicious anaemia owing to the very real risk (at least 30% of our cases) of neurological changes persisting or appearing for the first time—sometimes very acutely in the course of a few months. Therefore liver extracts or hog's stomach preparations must still always be employed in adequate dosage in treating pernicious anaemia with or without neurological changes, so that there is no indication for or advantage in using pteroylglutamic acid for this purpose. I deprecate very much the recurring efforts to offer "blunderbuss" mixtures of folic acid with liver, stomach, and iron—since they never contain any of the individual constituents in adequate therapeutic doses, the individual doses cannot be varied as required, and they are of no value in most blood diseases. On the other hand, in the other macrocytic and achrestic anaemias pteroylglutamic acid might sometimes be used with advantage, since neurological symptoms do not occur, although the cost is still an important feature.

The value of pteroylglutamic acid in treatment is also limited in the sprue syndrome, for patients with steatorrhoea and coeliac disease have given irregular response (from good to not at all) and have often required liver preparations to complete the clinical and haematological remission. The presence of a normoblastic marrow indicates that pteroylglutamic acid will be ineffective, since it is apparently effective only in the treatment of conditions with megaloblastic erythropoiesis. From the evidence it is quite clear that, whatever the part played by pteroylglutamic acid in erythropoiesis, there must be at least another factor concerned with the prevention and cure of the neurological features in pernicious anaemia, as I have suggested from my experience with hog's stomach preparations in the treatment of subacute combined degeneration of the cord and pernicious anaemia (Wilkinson, 1933). The role of pteroylglutamic acid in haemopoiesis is of course not at all clear, and we are still very short of clear-cut unequivocal facts.

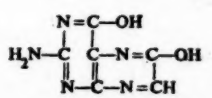
It was observed by Stokes (1944a, 1944b) from substitution experiments on the growth of *L. casei* and *Str. faecalis*, that folic acid could be replaced by certain pyrimidines and purines; of these, thymine (5-methyluracil) in a 5,000-fold concentration was effective. Taking up this observation, Spies *et al.* (1946, 1947) found that 7–15 g. of thymine daily was required to produce reasonably good haematological and clinical improvement, which was certainly not so good as with pteroylglutamic acid; it failed to prevent or relieve any neurological changes, glossitis, and stomatitis.

No haematological responses followed administration of many purines, pyrimidines, and members of the vitamin B complex, and Spies thinks the 5-methyl group in thymine has specificity of some kind in haemopoiesis (Spies *et al.*, 1945).

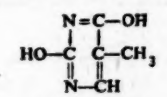
In past years I have also tried, with and without incubation with gastric juice or haemopoietin, many of the constituents of the vitamin B group, such as riboflavin, aneurin,



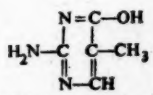
Pteroylglutamic Acid (Folic Acid)



Xanthopterin



5-Methyluracil (Thymine)



5-Methyl*iso*cytosine

pyridoxin, pantothenic acid, and xanthopterin, with negative results; the similarity between pteroylglutamic acid and 5-methyl*iso*cytosine led to a trial of this substance in doses of 100–200 mg. intravenously, and 5 g. orally, per day. With these doses slight reticulocytosis and a slow rise in the number of red cells and in haemoglobin percentage were obtained—results similar to those with thymine in similar dosage—and maybe larger doses are required to give full remissions.

It is perfectly obvious that pteroylglutamic acid is not: (*a*) the extrinsic factor of Castle (it can be given parenterally without the need for digestion with gastric juice); (*b*) haemopoietin, the anti-pernicious-anaemia stomach enzyme (Wilkinson and Klein, 1932); (*c*) the liver anti-pernicious-anaemia principle, which is highly potent in very small doses free from pteroylglutamic acid—thus, on the basis of dosage, 10–20 mg. of pteroylglutamic acid is required daily, while the maximal amount of it present in the corresponding dose of liver extracts is of the order of 0.02–3.7 μg. (i.e., a 5,000–20,000-fold difference) (Clark, 1945); pteroylglutamic acid will not mature marrow cells if incubated with them to form normal red cells from the precursors, although liver extracts will do so; or (*d*) the anti-subacute-combined-degeneration factor, whether it is or is not a different or separate factor from the anti-anaemia factor.

While free folic acid itself is almost universally active in relation to bacterial growth and the relief of chick, animal, and human anaemias and certain rat leucopenias, this is not so with the so-called vitamin B_c conjugates or pteroylglutamic acid conjugates. These conjugates consist essentially of pteroylglutamic acid combined with extra glutamic acid molecules to form polyglutamates, which are not universally active like the free folic or pteroylglutamic acid until the extra glutamic acid molecules have been removed by enzyme action or incubation with *Str. faecalis*. Nevertheless where they do act—as when given to rats, chicks, or monkeys suffering from *L. casei* factor, "vitamin B_c" deficiency, or "vitamin M" deficiency, respectively—their activities are proportional to their respective free folic acid contents.

The two crystalline polyglutamates so far examined are: (1) the vitamin B_c conjugate prepared from yeast (pteroylhexaglutamyl-glutamic or pteroylheptaglutamic acid), which has no effect on the growth of *L. casei* and *Str. faecalis*, and (2) the fermentation or *L. casei* factor (pteroylglutamic acid conjugate), obtained by the extraction of certain corynebacteria residues as pteroyl-diglutamyl-glutamic (or pteroyl-triglutamic acid), which promotes the growth of *L. casei*, but is only 1/50 as active as *Str. faecalis*.

It has been suggested that patients with pernicious anaemia are able to utilize only free pteroylglutamic acid and not the polyglutamates, probably owing to the gastric deficiency (Bethell *et al.*, 1947; Heinle *et al.*, 1947), while patients with other macrocytic anaemias having normal gastric secretions could use the polyglutamates. Spies (1946a, 1946b) claims that the doses the above authors employed were too small, and he has obtained moderate haematological responses in pernicious anaemia using the natural polyglutamates and also one synthetic diglutamate. Others (e.g., Sharp *et al.*, 1947) have also obtained responses with natural conjugates. This requires further confirmation using synthetic conjugates, as it is of the greatest importance.

Chicks, dogs, rats, and monkeys apparently utilize the polyglutamates because the pteroylglutamic acid is liberated by certain enzymes present in their livers or kidneys and probably by enzymes or bacteria in their intestinal tracts. It is difficult to believe that the human organs behave so differently from these. In fact, Denko *et al.* (1946) have shown that folic acid can be synthetized in quite large amounts in the human gut.

Summary

The relationship of "folic acid" (pteroylglutamic acid) and the "folic acid conjugates" (pteroyltriglutamic and pteroylheptaglutamic acids) are considered with their effects on the haematological changes induced in chicks, rats, and monkeys.

The uses of synthetic pteroylglutamic acid in the oral and parenteral treatment of certain diseases involving the haemopoietic system in man are described.

Pteroylglutamic acid produces good haematological and clinical effects only in macrocytic anaemias with some degree of megaloblastic change in the bone marrows; it has little or no effect on patients with normoblastic marrows. Consequently the following anaemias respond to pteroylglutamic acid: pernicious anaemia; macrocytic megaloblastic anaemias of pregnancy, infancy, pellagra, sprue, steatorrhoea, and coeliac disease; nutritional macrocytic anaemias (with or without nutritional leucopenia), and possibly achrestic anaemia.

Pteroylglutamic acid acts equally well when given orally or parenterally and has no ill effects on the patient. The initial dose varies with the individual patient, but is usually 15–20 mg. a day orally, or 50–150 mg. intravenously.

In pernicious anaemia a prompt reticulocyte response is produced after the administration of pteroylglutamic acid, followed by general haematological and clinical improvement, but not quite so well or so rapidly as with a highly potent liver extract. A maintenance treatment of 5–20 mg. daily is necessary, but after months of treatment a lower dose often shows a fall in the blood count and haemoglobin that will often respond to increased doses. Macrocytosis still tends to persist even after one to two years' treatment.

Pteroylglutamic acid is of no value in preventing the onset and progression or the development (which may be acute) of subacute combined degeneration of the cord in pernicious anaemia. For this reason it is not a satisfactory treatment for pernicious anaemia, and, since it has no advantages over present-day highly potent liver extracts or stomach preparations, it should not be given alone as routine to patients with pernicious anaemia.

Refractory macrocytic normoblastic anaemias do not respond to pteroylglutamic acid, but refractory megaloblastic anaemia may give responses.

It often relieves the symptoms of the sprue syndrome, leading to better-formed stools and some improvement in blood count, but only in the megaloblastic cases: the responses are irregular in steatorrhoea, and liver extracts may be required additionally to produce complete remissions. The response in coeliac disease may be very slow or poor; those with normoblastic marrows do not respond, since pteroylglutamic acid is effective only where megaloblastic erythropoiesis is present.

Pteroylglutamic acid has no beneficial clinical or haematological effects on hypochromic microcytic anaemias, haemolytic anaemias, refractory megalocytic anaemias with normoblastic marrows, acute and chronic leukaemias of all types, leucoerythroblastic anaemia, chronic ulcerative colitis, anaemias secondary to myxoedema or hyperthyroidism, toxic or idiopathic aplastic and hypoplastic anaemias, agranulocytosis, neutropenias, and thrombocytopenic purpura, but it relieves leucopenia and thrombocytopenia when these are features of a nutritional deficiency or a megaloblastic anaemia.

There is no place in therapeutics for the "blunderbuss" preparations of pteroylglutamic acid plus iron, liver extract, etc.

Pteroylglutamic acid is not the extrinsic factor, haemopoietin (the stomach enzyme or intrinsic factor), or the liver anti-pernicious-anaemia principle, nor is it the possible "neuropoietic" principle (anti-subacute combined degeneration of the cord). The effects of pteroylglutamic acid on haemopoiesis are discussed.

There may possibly be a separate factor in liver and hog's stomach preparations with neuropoietic properties for preventing or curing the neurological symptoms in pernicious anaemia.

The anti-pernicious-anaemia potencies of substances related to pteroylglutamic acid are considered.

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CONGENITAL MEGACOLON

RESULTS OF TREATMENT BY SPINAL ANAESTHESIA

BY

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In the milder cases of megacolon in childhood it may be that diet and medical measures will secure a sufficient action of the bowel, but where diet and drugs alike fail and frequent recourse has to be had to enemata and mechanical evacuation the need for surgical treatment is clear. Without such treatment the trouble tends to worsen, and in the more severe forms death is likely before the age of 20.

The fashion of surgical intervention has changed from time to time. In earlier days short-circuiting operations were tried and found wanting, while heroic resections of the dilated colon were attended by a high mortality even in experienced hands: 25% by Adson (1937). The mortality should certainly be lower to-day as a result of the better pre-operative preparation of the patient and his colon. There is undoubtedly a place for resection in the most severe varieties of the trouble which show no response to other forms of treatment.

The conception that megacolon is due to an achalasia—i.e., an imbalance between the sympathetic (filling) and the parasympathetic (emptying) mechanism which results in a relative inadequacy of the latter action—at once altered the outlook by suggesting an attack on the nerve supply rather than on the bowel itself. The sympathetic supply was interrupted in various places by bilateral lumbar, unilateral lumbar, presacral, and inferior mesenteric sympathectomies. On the whole, good results were obtained at small risk. But in 1935 Stabins, Morton, and Scott showed that success followed the use of a spinal anaesthetic alone. Since that date a number of successful results have been reported by various workers. These reports are open to criticism in that the follow-up period is too short. We have therefore re-examined those patients who were treated by spinal anaesthesia in the neurovascular clinic of the Manchester Royal Infirmary between the years 1938 and 1945. Cases treated within the last two years have been rejected as being too recent to be included.

The number of patients treated during the period is 17. We saw 11 of these patients during December, 1947, and obtained a detailed account of another: five were not traced. These 12 children comprised seven boys and five girls. The youngest was aged 6 months and the oldest 13 years when treated. The average age of the group was 7 years.

Technique

Apart from considerations of safety and control, the drug and method used for the spinal anaesthetic are immaterial. The point is that the effect must reach as high as the anterior roots of T.5 in order to abolish all activity in the splanchnic nerves. To make sure of this it is usual to allow the level of the anaesthesia to rise to the third thoracic segment or even higher, until tingling is felt on the inner side of the hand (T.1). The state of relaxation of the rectus abdominis is a good guide to the paralysis of the anterior roots; the muscle should be flaccid throughout so that the epigastrium bulges when the child cries or coughs.

After-treatment is important, and we have found the following regime to be satisfactory. Liquid paraffin is given daily in one dose of 1/2 oz. (14 ml.), and the enemata are administered every second day during the first week, twice during the second week, and once during the third. Enemata are then discontinued, but liquid paraffin is given in gradually reduced doses for as long as may seem necessary.

Results

The result has been classified as "good" in cases where the bowel action has become normal, "fair" when a considerable improvement has resulted but medicine is still required to maintain regular action, and "failed" when no worth-while improvement has been seen. The 12 cases are grouped as follows: good 8, fair 2, failed 2.

These cases were of a severe type and showed intractable constipation, physical under-development, "pie-crust" complexion, and mental lethargy—all features which mark the more serious forms of the disease. In the successful cases the parents have noticed that the children become much more energetic physically and much brighter mentally, often taking a better place at school. The improvement in growth, in development, and in complexion is striking to the observer. Four of the eight cured cases were treated not less than nine years before, and over this long period their bowel action has remained normal and unaltered.

Lumbar sympathectomy was done in three of the four unsatisfactory cases from one to two years after the spinal anaesthesia, but in only one of these did any further improvement result. It seems likely that cases in which a spinal anaesthetic has failed to produce improvement will also prove refractory to sympathectomy.

Discussion

The explanation of the results obtained in the megacolon of childhood from spinal anaesthesia remains a mystery, and the method must at present be regarded as purely empirical. For some reason the shock of the anaesthetic abolishes the imbalance between the sympathetic and parasympathetic supply of the colon. One can only assert that the method is simple and that it works. We believe that good results are more certain in the younger patients, and that 12 years would seem to be the upper age limit for success. The method is useless in the megacolon of adults, usually mechanical in origin, and in cases of ptosis with constipation in young women.

It is worth while to remember that in cases of megacolon the intra-abdominal scybalous mass, together with the general ill-health and malnutrition, may suggest a diagnosis of tabes mesenterica. In fact, of the present series no fewer than four were salvaged from sanatoria.

Finally, we must emphasize that there may be a delay of several weeks after the administration of the spinal anaesthetic before any improvement is manifest. Failure to realize this has doubtless been the cause of the supposedly poor results which some have had with the method. Later follow-up is likely to reveal a great improvement of which there was no sign during the stay in hospital (Hawksley, 1944).

Summary

The late results of cases of megacolon treated with spinal anaesthesia from two to nine years previously are reported. Out of 12 cases eight were found to remain fully cured.

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MEGALOBLASTIC ANAEMIA OF PREGNANCY

REPORT OF AN UNUSUAL CASE

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In recent years considerable attention has been paid to macrocytic anaemia of pregnancy. In 1938 Stevenson reported a series of 30 cases, and since then over 80 cases have been described by other investigators in this country (Davidson, Davis, and Innes, 1942; Lescher, 1942; Miller and Studdert, 1942; Fullerton, 1943; Callender, 1944). The term "megaloblastic anaemia of pregnancy" was suggested by Davidson, Davis, and Innes (1942) to replace "pernicious anaemia of pregnancy," since many of the criteria of true Addison's anaemia were not found in their cases. Callender (1944), while emphasizing the variability of the findings in this disease, considered two necessary diagnostic features to be "the presence of true megaloblasts in the peripheral blood and the demonstration of a megaloblastic change in the bone marrow."

The case reported below presents features which we have not been able to find in the literature and which we consider make it worthy of publication.

Case Report

A primipara aged 21 was delivered on Nov. 25, 1946, of a healthy female infant at an L.C.C. hospital. There was a second-degree primary tear, which was sutured. The antenatal history was negative, except that the patient was pale throughout pregnancy and had a persistent cough. She became pyrexial on Nov. 26; sulphadiazine and penicillin were given, but pyrexia continued. The haemoglobin on the 27th was 41%. She was transferred to the North-Western Hospital puerperal sepsis unit on Nov. 29.

On admission she was very pale and had a septic second-degree tear of the perineum, with a septic and lacerated cervix, but a normally involuting uterus. The spleen was palpable. Cultures from the cervix yielded no significant growth, and urine and blood cultures were sterile. A blood count (see Table I) showed marked anaemia, and she was transfused slowly with 1 litre of blood. The blood count, however, showed no improvement after the transfusion. Sternal puncture was performed on Dec. 3. In spite of penicillin treatment (30,000 units three-hourly) pyrexia persisted and numerous small pustules developed on the wrists and arms. Later, retinal haemorrhages occurred. Intensive liver treatment was started on Dec. 13, and a further blood transfusion was given with but little effect. The patient died suddenly on Dec. 31.

Haematological Findings

The first blood count on Nov. 30 showed a profound anaemia (haemoglobin 35%), and the white blood cells were decreased, with a high proportion of immature granulocytes. As the

TABLE I

Date	R.B.C. per c.mm.	Hb % (100% = 14 g.)	C.I.	W.B.C. per c.mm.	Differential %									Nucleated R.B.C. per 100 W.B.C.	Retics. %
					Neut.	Eos.	Bas.	Lymph.	Mon.	Met.	Myel.	Promyel.	My'bl.		
30/11/46	1,790,000	35	1	5,000	37	—	—	36	—	—	27	—	—	14	
3/12/46	1,790,000	34	1	4,000	21	—	—	21	—	2	13	36	7	17	
5/12/46	1,640,000	36	1·02	4,500	26	—	—	50	—	—	5	3	16	11	
6/12/46	1,740,000	35	1	4,000	41·5	—	—	35	—	1·5	1·5	3·5	17	6	
7/12/46	—	36	—	3,500	50	—	—	24	—	2	4	3	17	13	
9/12/46	2,010,000	36	0·9	3,500	43	—	—	12	3	4	4	12	22	12	
10/12/46	1,780,000	35	1	4,500	46	—	—	29	—	2	1	3	19	26	
11/12/46	1,460,000	27	0·96	5,500	48	—	—	31	2	1	8	2	8	10	
12/12/46	—	31	—	3,000	25	—	—	50	—	1	2	4	18	30	
13/12/46	1,480,000	30	1	3,000	30	—	—	48	—	1	—	5	16	39	
16/12/46	1,540,000	34	1·1	3,000	34	—	—	39	2	9	5	5	6	108	6
18/12/46	1,420,000	31	1·1	3,500	21	—	—	44	3	5	8	11	8	156	6
19/12/46	1,280,000	28	1·1	2,500	25	—	—	56	2	1	3	—	13	170	11
20/12/46	1,290,000	26	1·08	3,000	23	—	—	63	1	1	1	3	8	125	11
21/12/46	1,270,000	26	1·04	2,700	23	—	—	44	3	9	7	8	6	163	6
23/12/46	800,000	18	1·01	1,700	16	—	—	68	2	1	—	—	13	132	5
24/12/46	1,370,000	26	1·06	1,100	20	—	—	71	—	—	—	3	6	63	1
25/12/46	1,110,000	24	1	2,700	20	—	—	64	—	—	—	4	12	10	<1
26/12/46	1,114,000	22	1	1,700	10	—	—	84	—	—	2	2	2	14	<1
27/12/46	1,080,000	23	1·04	1,300	6·5	—	—	81	1	1·5	3	3	4	52	1
28/12/46	1,050,000	22	1·05	1,000	15	2	—	64	1	9	6	3	—	84	3
30/12/46	1,000,000	22	1·1	1,500	10	—	—	77	2	—	—	6	5	63	1

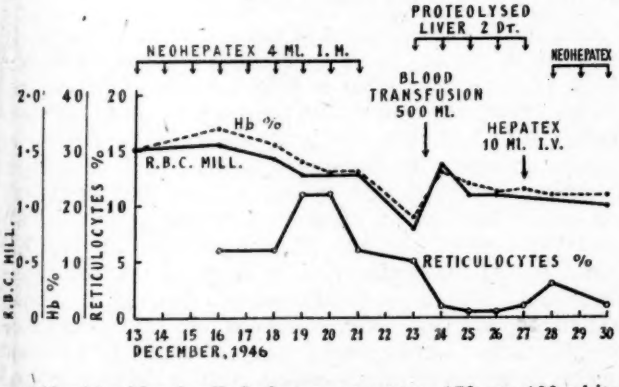
patient had sulphadiazine before admission it was thought that the drug might have depressed granulocyte production. When, however, the blood showed no improvement after transfusion and the white cells became more immature the possibility of acute leukaemia was suggested and sternal puncture was performed with the following results :

Total nucleated cells, 89,000 per c.mm.

	N.	E.	B.
Polymorphs	5	—	—
Metamyelocytes	3	—	—
Myelocytes	20	—	—
Promyelocytes	7		
Myeloblasts	22		
Lymphocytes	5		
Normoblasts, late	12		
,, intermediate	10		
,, early	2		
Megaloblasts, late	2		
,, intermediate	8		
,, early	4		
Proerythroblasts	0		

Myeloid/erythroblast ratio = 1.5 : 1

Since these findings did not confirm the diagnosis of leukaemia, and in view of the high erythroblast ratio with the presence of megaloblasts, a tentative diagnosis of liver-deficiency anaemia with coincident failure of maturation of the granular series was made. Intramuscular injections of "neohepatex," 4 ml. daily, were given, but after seven days the reticulocytes were only 11% (i.e., about one-third of the expected response) and the red blood cells and haemoglobin showed a continuous slight fall (see Chart). Nucleated red blood cells rose from 30



per 100 white blood cells before treatment to 170 per 100 white blood cells at the peak of the reticulocyte crisis (see Table II). There was no reduction in platelets during the period of observation. After 10 days' treatment the red blood cells had fallen to 800,000 per c.mm. and haemoglobin to 18%. A second transfusion of 500 ml. of blood was given, and neohepatex was replaced by proteolysed liver, 7 ml. daily by mouth (Davis and Davidson, 1944). The proteolysed liver appeared to be less effective than the neohepatex. Accordingly a single dose of hepatex, 10 ml., was injected intramuscularly and this was followed by 4 ml. of neohepatex daily. There was no response, however, to either preparation before the sudden death of the patient.

TABLE II.—*Differential Nucleated Red Count*

Date	Proerythroblasts	Megaloblasts	Normoblasts	Total per 100 W.B.C.
9/12/46	—	2	10	12
10/12/46	—	10	16	26
11/12/46	—	1	9	10
12/12/46	—	4	26	30
13/12/46	—	6	33	39
16/12/46	1	12	95	108
18/12/46	5	11	140	156
19/12/46	1	14	155	170
20/12/46	—	15	110	125
21/12/46	—	18	145	163
23/12/46	—	26	106	132
24/12/46	—	18	45	63
25/12/46	—	4	6	10
26/12/46	—	8	6	14
27/12/46	—	18	34	52
28/12/46	—	11	73	84
30/12/46	—	5	58	63

Post-mortem Findings

Permission for necropsy was not granted till 48 hours after death, and post-mortem change was advanced in all organs. There was caseous tuberculosis of the hilar glands and a caseous tuberculous focus, 1 cm. in diameter, in the lower lobe of the right lung. The heart muscle was thin, pale, and flabby, with a few subpericardial haemorrhages. The spleen (450 g.) was congested and friable. The liver (3,000 g.) was pale and rather greasy. The uterus showed some necrosis of the placental site but was well involuted. Apart from generalized pallor there was little of pathological importance in the other organs. The bone marrow of the sternum, ribs, and femur was a rich dark-red colour. Sections and films of sternal marrow showed an extreme cellularity, the predominant cell being of the primitive haemocytoblast variety with large numbers of megaloblasts (mostly early) and normoblasts. Granulocytes and their precursors were almost completely absent. Megakaryocytes were numerous. As the patient died unexpectedly in the evening and marrow puncture was not done till next day, the cells were somewhat degenerate.

Discussion

In the various reports of cases already quoted little mention is made of any changes in the white blood cells. Callender (1944) found a leucopenia common with "myelocytes and young forms." Other writers record low total white blood cells but give no differential counts. We have been unable to find any reference to such profound immaturity of the white blood cells in the peripheral blood in any other cases of megaloblastic anaemia of pregnancy, although myeloblasts are occasionally found in the peripheral blood in pernicious anaemia (Whitby and Britton, 1946). In our patient leucopenia was constant and the white blood cells decreased gradually from 5,000 to 1,500 per c.mm. the day before death. Myelocytes,

promyelocytes, and myeloblasts formed from about 20 to 50% of the total for the first two weeks, gradually falling with the count (Table I). It has already been mentioned that the question of agranulocytosis following sulphadiazine was raised after the first count. In our experience, however, it is unusual to find early granulocytes in the peripheral blood in agranulocytosis except during recovery. Generally the polymorphs drop suddenly without warning, and no precursors reach the peripheral blood until regeneration of the marrow is taking place. In this case, also, only 8 g. of sulphadiazine had been given. The alternative suggestion of acute leukaemia appeared at first to fit the severe anaemia with myeloblasts in the peripheral blood, but sternal puncture did not confirm this. The findings of a definite megaloblastic reaction in the marrow suggested rather a deficiency of the haemopoietic principle, and it seemed probable that this was the primary abnormality and that the high proportion of myeloblasts was due to a coincident failure of maturation of the granulocytes rather than a true leukaemic change.

Although liver therapy was not begun until a late stage in the disease, the poor response to the three preparations used seems to indicate the refractory nature of the anaemia. Defective absorption from the intestine may have been partly responsible for producing the anaemia, since proteolysed liver was even less effective than neohepatex. Nutritional deficiency might also account for the failure in maturation of the granulocytes.

Summary

A case of megaloblastic anaemia of pregnancy is described.

An unusual feature was the marked immaturity of the circulating granulocytes simulating an acute myeloblastic leukaemia.

The case proved refractory to various types of liver therapy and to blood transfusion.

ADDENDUM

Since the completion of this paper, blood and sternal marrow films were referred to one of us (M.G.) from another L.C.C. hospital for diagnosis. The patient, a married woman aged 34, had been treated by her doctor for acute tonsillitis and various other complaints with 70 g. of a sulphonamide over a period of five weeks. On admission she complained of giddiness and faintness of two weeks' duration, and her blood count on Dec. 8, 1947, was : red blood cells, 1,000,000 per c.mm. ; haemoglobin (Sahli), 24% ; colour index, 1.2 ; white blood cells, 13,000 per c.mm. (neutrophil polymorphs 9%, promyelocytes 77%, myeloblasts 14%) ; mean cell diameter 7.8 μ ; nucleated red blood cells, 21 per 100 white blood cells (normoblasts 15, megaloblasts 6) ; anisocytosis + +, poikilocytosis +, polychromasia + +.

The patient was transfused with 2 pints (1.14 litres) of blood, and on Dec. 10 the sternal marrow films showed the following distribution :

Neutrophil polymorphs	1.5%
Metamyelocytes	0.0%
Myelocytes	0.5%
Promyelocytes	30.0%
Myeloblasts	11.0%
Lymphocytes	4.0%
Normoblasts, late	7.5%
,, intermediate	2.5%
,, early	0.0%
Megaloblasts, late	11.5%
,, intermediate	20.0%
,, early	9.5%
Proerythroblasts	2.0%

Myeloid/erythroblast ratio = 1 : 1.2

Since both the peripheral blood and marrow resembled the case described above the patient was treated with liver and iron but showed no reticulocyte response. After two further transfusions on Dec. 12 and 17 her red blood cells rose to 3,800,000 per c.mm. and haemoglobin to 73%. Although she was given penicillin throughout her stay in hospital she developed pneumonia on Dec. 19 with Friedländer's bacillus and *Ps. pyocyanea* in the sputum. The blood count was maintained without further transfusion and the white cells, which had dropped to 750 per c.mm. on Dec. 20, rose to 9,000 per c.mm. on the 24th, with a much lower percentage of primitive cells. The patient died on Dec. 25. Post-mortem examination showed bronchopneumonia and an extremely cellular bone marrow. Sections showed the majority of cells to be of the red cell series and apparently megaloblastic.

The similarity between the two cases is striking. Both showed extreme anaemia with megaloblasts and primitive white cells in the peripheral blood and a megaloblastic reaction in the marrow, and both failed to respond to liver. Aetiologically, however, the two cases differed : in the first case pregnancy, and in the second the excessive dosage of sulphonamide, were apparently the main contributory factors.

We are indebted to Dr. R. D. Green, of Paddington Hospital, for the clinical notes of the second case.

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HEREDITARY OEDEMA (MILROY'S DISEASE)

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Reports on a heredo-familial variety of oedema of the lower limbs were published almost simultaneously by Nonne (1891) and Milroy (1892). A few years later Meige (1899) reported a further series of cases. The condition described as hereditary oedema, or eponymously as Milroy–Nonne–Meige disease, has since been recognized as a distinct clinical entity, having been recorded by many physicians in various countries. References in British literature have, however, been relatively scanty, the only one in recent years being that of Weber and Schlüter (1937). The main features of Milroy's disease are here summarized.

Aetiology.—The disease is hereditary. Milroy's original family of 97 persons in six generations presented 22 cases. Meige reported eight cases in four generations, Hope and French (1907) 13 cases in five generations of 42 persons. Gates (1946), analysing the family described by Hope and French, considers the hereditary trait to be a Mendelian dominant, but notes that in one affected person it was transmitted through an apparently normal mother. Two unaffected mothers in the third generation of Milroy's family passed the tendency on to some of their offspring. Such a skipping of a generation is common in human dominant pedigrees. Both sexes are affected. The cause of the oedema is not known ; it is not related to the usual general or local causes of oedema, such as cardiac or renal disease, venous or lymphatic obstruction. Meige postulated a "congenital malformation of trophic centres in the spinal cord," though this has never been proved. Hope and French compare the disease with other heredo-familial disorders of the vasomotor system, such as angioneurotic oedema, Raynaud's phenomenon, and urticaria, and suggest that it may be a "vasomotor neurosis." Milroy (1928), in a review of the condition

agrees with this point of view, favouring a local cause, such as an abnormality of function of veins or lymphatics, of neurogenic origin.

Pathology.—A necropsy has not yet been recorded on a case of Milroy's disease, and the only microscopical study which appears in the literature is that of McGuire and Zeek (1932), who report the results of biopsy in a typical case. Microscopy of a portion of the skin and subcutaneous tissue showed a normal epidermis but a marked condensation of the superficial portion of the dermal papillary layer composed of fine collagen fibrils which in some places were undergoing hyalinization; oedema was more pronounced in the dermis, and this, together with an increase of collagen fibres, produced a great increase in the proportion of dermis to epidermis. There was a considerable sprinkling of lymphocytes related to the capillaries and venules. The subcutaneous tissue was also thickened, consisting of masses of oedematous fatty tissue and pools of colourless fluid not contained within definite limiting boundaries. The appearance contrasted with that of fresh necropsy material obtained from cases of cardiac and renal dropsy; in these the dermal papillae were flattened and much less obvious.

Clinical Features.—The age of onset varies in the different families recorded. In Milroy's series all but two showed oedema at birth. In one of these two the oedema started at the age of 12; in the other, one swollen foot was present at birth, the other limb being normal until the age of 20, when, following an injury, it became rapidly and permanently swollen. All of Meige's cases had their onset at puberty. In the family recorded by Hope and French (1907) oedema began in infancy, childhood, or adolescence As each author has described a single family, differences in age of onset and other features may, as Milroy (1928) pointed out, be considered to be familial variations of an essentially identical disorder.

The oedema begins in the toes, gradually spreads up the limb, but never extends above the level of the inguinal ligament, where it is sharply demarcated; it may remain at lower levels, especially joints, for long periods. At first the oedema pits readily on pressure, though later the tissues become more indurated and thickened, and is reduced by rest with elevation of the limb. One or both limbs may be affected. There are no constitutional disturbances and the disorder is compatible with long life. Another remarkable feature of the condition is the absence of disability; in spite of grossly swollen limbs affected persons may be quite capable of a normal existence. One of Milroy's (1928) patients was a Burma missionary who wrote that he found no difficulty in tramping distances of 30 miles a day over rough mountain track. The oedema appears to be permanent, with the remarkable exception of another of the cases mentioned by Milroy (1892) (unfortunately not seen by Milroy himself). This patient was born with oedema of one foot, and at puberty developed swelling of the testicles which became sufficiently great to necessitate orchidectomy, and at the same time the swelling of the foot disappeared.

In addition to the above clinical features Hope and French (1907) described acute attacks in many of their patients in which the affected limbs suddenly became red, painful, tender, and much more swollen; there was no obvious cause for the onset or remissions of these attacks.

Treatment.—Because of the minimal symptoms there is usually no indication of any treatment other than bandaging to control the size of the limb. Among patients with oedema of the limb treated by the Kondoleon operation Sistrunk (1918) records two cases with oedema of the lower limb in which the clinical histories suggest a diagnosis of Milroy's disease; good results were obtained, and this suggests that surgery may be useful if there is serious disability.

Case Report

An apprentice engineer aged 19 was referred by Dr. Hugh Garland from his out-patient clinic at the General Infirmary at Leeds and admitted to St. James's Hospital, Leeds, complaining of swelling of his right leg and his scrotum. He had had no previous major illness. There was no history of "allergic" disease or of infection in the legs. He had never been out of this country.

Family History.—The patient was the youngest of three children. His parents were not blood relatives. His elder sister, a housewife aged 24, had noticed swelling of her right leg when she was 14. Up to the age of 20 she had worked in a factory and the swelling was then severe at the end of the day, and at its worst had extended from ankle to knee. When seen by us the left leg appeared normal; the right leg showed a pitting oedema involving the ankle and the lower third of the right calf. There was no other evidence of disease of any kind. She had had no children. The younger sister, a housewife aged 22, had no history of oedema and no abnormality on examination. She had one child, a boy aged 2, with no abnormality. The father, aged 52, had no abnormality on examination. The mother, aged 45, one of twelve siblings, though showing no abnormality of the lower limbs on examination, herself asserted that since puberty she had noticed her ankles to be swollen at the end of a day's work. No history was obtained of any oedema of the limbs in preceding generations on either side, nor was there any history of familial disease.

History of Illness.—The patient first noticed swelling of his right ankle at the age of 17, which was painless and decreased at night after rest. It had gradually and steadily increased, spreading upwards to involve the whole of the leg. He had also noticed swelling of the scrotum, which he thought had begun at about the time the leg swelling had reached the groin. He thought the condition had been stationary for the four months before admission. Despite the size of the leg there had been little interference with function and he led a normal life. He had had no acute exacerbation of the condition, nor anything suggestive of infection in the leg. It seems that puberty had not been reached until the age of 17 and had roughly coincided with the onset of the oedema. He was shaving only once a week at 19.

On examination he was a slimly built youth who looked younger than his age. There was little facial, axillary, or pubic hair. The left leg was normal. There was massive pitting oedema of the right leg, sharply limited above by the inguinal ligament and fading towards the toes, which appeared normal when first seen. The colour and temperature of the limb were normal. There were no trophic disturbances of the skin and no enlarged veins. After he had worn slippers for two days the oedema spread into the toes. The scrotum was not oedematous. There was bilateral hydrocele, left larger than right. After the hydroceles were tapped the testicles were found to be bilaterally and symmetrically enlarged, and testicular sensation was much diminished. After complete rest in bed the oedema decreased steadily, the minimum size being reached in five days; it increased to its maximum in three days when the patient was allowed up again. (See illustration.)

Measurements

	On Admission				After 5 Days at Rest			
	Right		Left		Right		Left	
	in.	cm.	in.	cm.	in.	cm.	in.	cm.
Mid-foot	10	25·4	9	22·8	8¾	22·3	9	22·8
Ankle	12½	31·75	9	22·8	9	22·8	9	22·8
Calf 4 in. (10 cm.) below patella	16⅝	41·9	12	30·5	13⅝	34·5	12	30·5
Mid-thigh	20½	52·0	16	40·6	17½	44·5	16	40·6

Laboratory Tests.—Haemoglobin, 108%; leucocytes, 6,500 per c.mm. (44% polymorphs, 52% lymphocytes, 4% monocytes). Blood potassium, 21.2 mg. per 100 ml.; blood urea, 19 mg. per 100 ml.; serum protein, 7.7%; chlorides (as NaCl), 0.57%; creatinine, 1.7 mg. per 100 ml.; uric acid, 4 mg. per 100 ml. Glucose-tolerance test normal. Urine: S.G. 1026, acid; no albumin, sugar, casts, or cells. Urinary chlorides, 7.4 g. in 24 hours. Fractional test meal, normal curve. Histamine

skin sensitivity test, no reaction. Radiograph of bones normal. Wassermann reaction negative.

Treatment.—The patient suffered very little disability from his oedema and was quite able to enjoy a normal life. He complained of some "tiredness" of the affected limb at the

end of the day, but despite this he would voluntarily indulge in gymnastic exercises after a full day's work. No surgical intervention was therefore advised. Firm bandaging had some effect in controlling the oedema and also gave him a feeling of support.

Discussion

Examples of unilateral or bilateral oedema of the extremities for which no obvious cause can be discovered are not infrequently encountered; cases with a clear hereditary or family history are, however, much less common, and few have been recorded in British medical literature. The question arises whether patients who display the typical oedema of one or both lower limbs as described above, but who lack the appropriate family history, should be regarded as suffering from Milroy's disease. In this connexion we note that Parkes Weber, discussing at a meeting of the Royal Society of Medicine a family of four sisters in whom oedema of the legs began between the ages of 20 and 23 (Weber and Schlüter, 1937), considered that if the other features were present a family history was not essential for the diagnosis, and for that reason preferred the eponym Nonne–Milroy's disease to the term hereditary oedema. However, the heredo-familial factor in the classical descriptions quoted above is so striking that it seems to justify a separate nomenclature for the hereditary and non-hereditary forms. In describing the aetiological factors it was noted that one unaffected person in the family reported by Hope and French (1907) and two unaffected persons in the family reported by Milroy (1892) produced affected offspring. Apart from these gaps, however, the line of inheritance is direct. It appears, therefore, that the responsible gene is transmitted as a Mendelian dominant with occasional skipping of a generation. In view of this possibility of skipping, the fact that the disease has been recognized for the first time in members of a particular generation does not rule out the likelihood that it has been handed down from earlier generations, especially when it is remembered that the manifestations may be minimal, easily missed by patient and doctor. (In the families described above there was considerable case variation in the degree of oedema, and this was also found in the family reported by us.) Alternatively the condition may arise as a mutation, though this is impossible to establish.

Apart from the description by Milroy (1892) of the patient with testicular enlargement and subsequent disappearance of the oedema, we have not discovered any record of a patient who, like the one we have reported, suffered also from hydrocele and testicular abnormality. While there seemed to be definite evidence of diminished testicular function, it is not clear that there was any relation between this and the oedema, nor would it justify in itself any suggestion that an endocrine factor plays a part in the production of the oedema. Although the disorder has been recognized for over fifty years, the ultimate mechanisms responsible for the chief symptoms remain obscure.

Summary

Milroy described a hereditary form of oedema of the lower limbs for which there was no obvious cause.

This condition produces little or no disability.

A typical case, with bilateral hydrocele and delayed puberty, is described.

We wish to acknowledge our thanks to Dr. Hugh Garland, consulting physician to St. James's Hospital, and to Dr. J. A. Fraser Roberts for much helpful advice and criticism. Dr. W. McIntosh, Medical Director of Leeds Municipal General Hospitals, kindly granted permission to publish this case. Our thanks are also due to Miss C. E. Campbell for the photograph.

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TWO CASES OF PERIARTERITIS NODOSA
WITH OBSERVATIONS ON AETIOLOGY, DIAGNOSIS, AND TREATMENT

BY

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Periarteritis nodosa was first described by Rokitansky in 1852. Kussmaul in 1866 related symptomatology to clinical findings, and during the next 76 years some 350 cases of the disease were reported. Here are recorded two further cases.

Case 1

This patient, a Merchant Navy man, aged 43, was admitted to the Western Infirmary, Glasgow, on Oct. 20, 1946. He complained of an aching pain in the muscles of his back and legs, epigastric discomfort, anorexia, and loss of weight for four weeks. This had been associated with a low-grade pyrexia. He had had malaria in 1938, and in 1939 was treated for staphylococcal empyema by rib-resection and with sulphapyridine over a long period. Sulphonamides had also been administered three weeks and again three days before admission to the infirmary.

On admission the abdomen showed slight generalized distension. It was "doughy," and on palpation the epigastrium and

both lumbar regions were tender and rigid. The muscles of the legs were tender on pressure; no oedema was observed. No other physical abnormality was detected. Temperature was 99.2° F. (37.3° C.), pulse 105, and blood pressure 150/90. During the next 17 days his condition deteriorated. The temperature was intermittent, ranging from 97 to 101.5° F. (36.1 to 38.6° C.). The pulse rate varied from 80 to 115. Muscular and abdominal pains and increasing general weakness accompanied these changes. On Nov. 8, and for several days subsequently, painful subcutaneous nodules were present on the abdominal wall. One such nodule was removed for histological examination.

After Nov. 15 his general condition improved, although two further exacerbations occurred. On Nov. 22 he complained of stiffness of the neck muscles and pain in the right testicle. On Nov. 19 pain in the lower left chest and left hypochondrium was accompanied by splenic enlargement. During this time the temperature continued to range between 97 and 101° F., and the pulse rate between 70 and 120. The erythrocyte sedimentation rate varied between 37:70 and 75:106 (Westergren).

These acute manifestations subsided within a few days, and the patient continued to improve generally. On Jan. 11, 1947, he was apyrexial and symptom-free, and was discharged from hospital.

Investigations in Hospital.—Blood:—There was no evidence of anaemia. The white cell count varied from 27,200 to 11,000 per c.mm. The highest eosinophil reading reported was 5%. On Dec. 6 the serum albumin was estimated at 4.6% and total protein at 6.4%. The Wassermann reaction was negative. *Urine:*—No abnormal constituents were found. Despite repeated investigations, tests for albumin and red blood cells were uniformly negative. *Fractional test meal:*—A normal acid curve was obtained. Blood was present in the fasting juice, and a test for occult blood in the faeces was positive. *X-ray examination:*—Radiologically the lumbar spine, gall-bladder, chest, and arms revealed no abnormal features. Barium meal and enema investigation of stomach and bowel did not disclose any evidence of disease. *Ophthalmoscopic examination* (Nov. 23):—Prof. W. J. B. Riddell reported that no abnormality was detected in either fundus. An *electrocardiogram* (Nov. 23) showed slurring of QRS in leads I and III of a degree which is proof of myocardial change. *Proctoscopic examination* (Dec. 12) revealed no marked change in rectal mucosa. Excess mucus coming down from sigmoid was present; examination of this showed no abnormality. *Histology of subcutaneous nodule* (Nov. 14):—The report on the subcutaneous nodule removed from the abdominal wall was furnished by Dr. G. B. S. Roberts. It read: "The larger blood vessels show changes characteristic of periarteritis nodosa. There is fibrin present in the media and a gross collection of inflammatory cells, mainly polymorphs, in the adventitia."

Progress since Discharge from Hospital.—Since the patient was discharged from hospital (Jan. 11, 1947) three episodes of significance have occurred. (1) On Jan. 24 the patient's urine contained albumin, red blood cells, and granular casts. (2) On March 21 the patient complained of severe headaches, maximal in intensity over the vertex. On March 25 retinal haemorrhage in the left eye was reported, and on April 15 it was suggested that a further haemorrhage had occurred and that the vessel associated with this haemorrhage was raised from the retina. (3) On March 27 he complained of the passage of blood in his stools. This complaint persisted for three weeks. Further proctoscopic examination did not reveal any abnormal feature with the exception of a congested rectal mucosa. No specific pathogenic micro-organisms were isolated from a rectal swab. Bleeding time, clotting time, and blood film were within normal limits.

During this period of out-patient surveillance the condition of the myocardium improved, as shown by repeated electrocardiographic tracings. On Feb. 28 the electrocardiogram showed that slurring of QRS was not then of diagnostic significance.

Comment on Case 1.—The two main points of interest are: (1) the diagnosis was made during life, and (2) some thirteen months after discharge the patient is well enough to be in employment. The average duration of the disease is given by Leishman (1937) as between three and four months. Some cases, however, have been known to recover.

Case 2

A housekeeper aged 52 was admitted to the Western Infirmary, Glasgow, on Dec. 13, 1946, with a complaint of pain in the chest and haemoptysis of ten days' duration and loss of weight and general weakness for some nine months.

Previous History.—She had been under investigation in a county hospital from July to November, 1946. The history and investigations covering this part of her illness were as follows. Subsequent to an influenzal illness occurring over Christmas, 1945, she experienced weakness of her legs associated with pain in legs, arms, and back of neck. No sulphonamide drugs were given at this time. Her left ankle is stated to have been swollen, and anorexia was accompanied by considerable loss of weight. Clinical examination seems to have been largely negative. "Fibrous" nodules were reported to be present in the trapezius. Blood pressure was 120/80. The temperature varied between 97 and 101.5° F. (36.1 and 38.6° C.) and the pulse rate between 80 and 120, until mid-September, 1946, when both gradually settled to average levels. This was maintained until she was discharged on Nov. 9. The erythrocyte sedimentation rate remained elevated throughout this period—July, 93:115; October, 92:120. The following investigations were carried out: (1) Blood:—No evidence of anaemia present. The leucocyte count varied between 5,000 and 11,500 per c.mm. The highest eosinophil reading reported was 2%. (2) Urine.—Reaction acid; specific gravity, 1026. Albumin, trace. On microscopical examination 8 to 11 red blood cells were present per high-power field. (3) Fractional test meal:—A normal free-acid curve was obtained. A test for occult blood in the faeces was positive. (4) *X*-ray examination of chest, long bones, hands, and feet, barium meal, and barium enema revealed no gross lesions.

After being discharged home on Nov. 9, 1946, the patient remained in moderately good health until three weeks before admission to the Western Infirmary. At this time she developed herpes zoster of her right chest, and after a few days haemoptysis occurred. Recurrent vomiting was complained of for six days before admission to the infirmary.

On admission the patient looked very ill and was markedly emaciated. The percussion note over the right apex was impaired, and crepitant rales were present at the right apex, right mid-zone, and left base. The abdominal reflexes were not elicited; both ankle- and knee-jerks were very active; the plantar responses were flexor. The pulse rate varied between 80 and 120, the temperature between 97 and 98° F. (36.1 and 36.7° C.). The blood pressure was 118/75. The patient is stated to have suffered from "chest trouble" in adolescence. Her mother died of "chest trouble." Her father died of rheumatic fever at the age of 27.

A blood count showed: red cells, 2,100,000 per c.mm.; haemoglobin, 47%; white cells, 8,000 per c.mm. The erythrocyte sedimentation rate was 120:150. No abnormality was detected in the urine. Tubercle bacilli were not found in the sputum. An *x*-ray report of the chest on Dec. 13 was: "Old calcified primary lesions in both hilar regions and in right lower lobe. Mottled opacities right upper lobe. Appearances are suggestive of active tuberculosis. There is increase in transverse diameter of the heart."

On Dec. 17, four days after admission, the patient died suddenly.

Post-mortem Report.—A necropsy carried out by Dr. George Smith in the pathology department disclosed the presence of typical lesions of periarteritis nodosa in kidneys, liver, lungs, spleen, heart, small intestines, pancreas, adrenals, and uterus. While a few of the lesions were reported to be in the healing phase of fibrosis the great majority showed acute necrosing inflammation of the vessel wall with oedema and polymorph infiltration, in which eosinophils were noteworthy. The vessels chiefly affected were the small arteries and arterioles. With the exception of a healed calcified scar at the apex of the left lung no evidence of pulmonary tuberculosis was detected. Both lungs were denser in patches than normal, but the consistency was considered to be not that of fibrosis or neoplasm,

and was due to haemorrhage. Histological examination did not disclose the presence of tuberculous lesions in the lungs. The immediate cause of death was probably the severe damage to the kidneys. The femoral vein blood urea twelve hours after death was 129 mg. per 100 ml.

Comment on Case 2.—This case was not diagnosed until a post-mortem examination had been performed. The clinical diagnosis appeared to rest between pulmonary neoplasm and pulmonary tuberculosis. The latter possibility was supported by the result of *x*-ray examination of the chest, to which reference has been made. The interesting points in the case are: (1) The patient was a female suffering from a rare disease in which males are affected four times as often as females. (2) Haemoptysis is not a common symptom of periarteritis nodosa. It occurred in only 1% of cases in a series reviewed by Bruce Logue and Mullins (1946). (3) In Kline and Young's (1934) three cases the difficulty in differentiating periarteritis nodosa affecting the lungs from pulmonary tuberculosis was observed. Bruce Logue and Mullins (1946), referring to this, suggest that areas of fibrosis due to small infarctions may resemble pulmonary tuberculosis radiologically. In this case the findings both on clinical and on *x*-ray examination were compatible with a diagnosis of pulmonary tuberculosis.

Aetiology

The cause of periarteritis nodosa is not yet definitely known. Transmission of the disease to animals has been reported by Von Haun (1920) and by Harris and Friedrichs (1922). These results do not appear to have been obtained by other workers, although Muir (1940) considers the pathological picture to be compatible with the activity of an unknown infective agent.

Ophüls (1923) and Neale and Whitfield (1934) suggest that periarteritis nodosa is a manifestation of a streptococcal allergic state. Its association with rheumatic heart disease was noted by Friedberg and Cross (1934) in four of their eight cases, and they considered that the disease may result from hypersensitivity to more than one agent. This view has received the support of Anderson (1944). Eight cases of periarteritis nodosa associated with asthma and eosinophilia are reported by Rackemann and Greene (1939), and Rich (1942) records the development of periarteritis nodosa in cases which had shown evidence of hypersensitivity to serum or sulphonamides, or both. In 1943 Rich and Gregory demonstrated that the disease could be produced experimentally in rabbits by sensitizing them to foreign serum–sulphonamide complexes. In 1946 Bruce Logue and Mullins referred to a possible relationship between acute disseminated lupus erythematosus and periarteritis nodosa.

It would therefore seem that allergy plays a very considerable part in the aetiology of periarteritis nodosa, and, further, that a hypersensitive "soil" may be an essential factor in the development of the disease. In this connexion it is of interest to record that the son of Case 1 has been found to be suffering from Besnier's prurigo–eczema–asthma syndrome. Hypersensitivity to drugs of the sulphonamide series may be implicated in certain instances, and the apparently increasing incidence of the disease may be attributable to this fact. Sulphonamide drugs had been administered to Case 1 on several occasions. On the other hand, all inquiries regarding this aspect in Case 2 have been entirely negative. There can be little doubt that the disease existed before the sulphonamide era, and in some instances hypersensitivity to infective agents may be responsible.

Diagnosis

The possibility of periarteritis nodosa should be borne in mind in a case presenting multiple symptoms referable to several systems. In Case 1 the diagnosis initially seemed to be that of pyrexia of uncertain origin, with emphasis on the possibility of enteric fever and abdominal tuberculosis. With the appearance of cutaneous nodules, periarteritis nodosa, carcinomatosis, and trichiniasis became possibilities; less probable causes in this case being bacterial endocarditis with multiple emboli, and Weber–Christian syndrome (Weber, 1925; Christian, 1928). The combination of myositis, abdominal pain, loss of weight, tachycardia, and fever, associated with cutaneous nodules, suggested periarteritis nodosa, and this was confirmed by histological examination of a nodule.

The triad of myositis, abdominal pain, and loss of weight has been referred to by Meyer and by Middleton and McCarter (1935). In a review by Bruce Logue and Mullins (1946) tachycardia and fever occurred in 87%, abdominal pain in 56%, myositis in 44%, loss of weight in 44%, and cutaneous nodules in 23% of cases.

It is regrettable that no characteristic lesions are observed on ophthalmoscopic examination, but emphasis should be placed on histological examination of cutaneous nodules in suspected cases, or in their absence success may attend muscle biopsy.

Treatment

From a review of the literature no treatment appears to have been of any value. Leishman (1937) confirms this view. Assessment of any particular treatment is difficult because of the infrequency with which the disease is diagnosed during life. Secondly, chronic forms characterized by exacerbations and remissions occur (Arkin, 1930; Macaigue and Nicaud, 1932). Lastly, Boyd (1944) emphasizes the conception of healed periarteritis nodosa with multiple chronic ischaemic lesions.

Penicillin.—As long-continued pyrexia suggested infection in Case 1, penicillin was tried, a total dosage of 4 mega units being given intramuscularly from Dec. 4 to 10. Penicillin in smaller dosage had been administered to Case 2 before admission to the Western Infirmary, Glasgow. No improvement occurred in either case during or immediately subsequent to penicillin therapy. Despite this it is possible that beneficial effects might ensue in cases in which a penicillin-sensitive micro-organism is acting as antigen. On the other hand, according to Suchecki (1946), allergic reaction to penicillin occurs in some 0.5% of cases. In such instances penicillin therapy may indeed be contraindicated.

Anti-histamine Preparations

The drugs used were β-dimethylaminoethyl benzhydryl ether hydrochloride ("benadryl") and histamine azoprotein ("lertigon"). These were employed on the basis of the histamine concept of allergy. Benadryl has histamine antagonizing properties (Loew, Kaiser, and Moore, 1945). It is thought to act by competing with histamine for a given site of action, and thus prevents the effect of histamine combination at this site. On the other hand, lertigon is said to produce antibodies which neutralize histamine before it can enter into combination at the site of action. Benadryl and lertigon are thus synergistic in action, and it would appear rational to use them concurrently.

In Case 1 benadryl was administered initially in doses of 50 mg., four times daily, and its administration coincided with a tendency of the temperature and pulse rate to return to average levels. It would appear, however, that benadryl has not been effective in preventing the retinal and alimentary tract exacerbations (March, 1947). No toxic effects have been observed; but it was noticed that a steady fall in the patient's weight ceased when the dose of benadryl was reduced. No explanation has been found for this

side-effect of benadryl, if indeed the drug was responsible for the loss of weight.

Lertigon therapy was started in May, 1947, being administered subcutaneously in increasing doses every fourth day, up to a maximum single dose of 1 ml. Subsequently the dose has been reduced to 1 ml. weekly. No toxic effects have been observed.

Since beginning this combined therapy no exacerbations of the disease process have occurred. The patient states that he feels well, his weight is stationary, and the erythrocyte sedimentation rate is within average limits. There is some evidence, however, that hypertension may be developing, possibly secondary to ischaemic renal lesions. Whilst no conclusions can be drawn from a single case, it is felt that therapy along similar lines may hold out promise for the future treatment of periarteritis nodosa, and perhaps of other conditions.

Summary

Two cases of periarteritis nodosa are reported. One case was diagnosed during life, and 16 months after admission the patient is in good health. The aetiology of the disease is reviewed. It would appear that periarteritis nodosa is an expression of an allergic state to either micro-organisms or drugs—e.g., sulphonamides.

Observations are made regarding diagnosis. Emphasis is placed on clinical diagnosis, and the importance of histological examination of cutaneous nodules or muscle tissue in any doubtful case is stressed.

The results of treatment with penicillin, benadryl, and lertigon are reported. Encouraging results have followed combined benadryl and lertigon therapy in one case.

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Mr. James Griffiths, Minister of National Insurance, points out in a message he has sent to all members of the staff of his department that 700 of the 1,000 local national-insurance offices ultimately needed are already open and the necessary wide and intimate contacts with the public have already begun. He adds: "We must never forget that for the most part we shall be dealing with people who are ill or in trouble or are perplexed by some point or other. They will need not only the benefits due to them but in many cases help and advice also. There have already been many difficulties and there will be more. We are compelled to go forward in face of shortages of premises, of staff, and of equipment of every kind. Success must depend not only on the initiative and leadership of those in key positions but also on an alert and willing response from all. I have found everywhere the keenest enthusiasm and a high sense of the great social mission with which the Ministry is charged. This is going to be a soldier's battle for us and I am confident that every member of the staff, from the highest to the lowest, will do his best and not spare himself in the critical months that lie ahead of us."

Medical Memoranda

Otitis Media in Infancy

The following brief statistical survey indicates that otitis media in infancy remains a major clinical problem in a large children's hospital. It shows the results of treatment with penicillin and sulphonamides and of the surgical procedures of myringotomy and posterior drainage of the mastoid antrum.

Of 7,806 admissions to the wards of Alder Hey Children's Hospital, Liverpool, during the year 1946, 1,107 were infants under the age of 12 months. This number includes medical, surgical, and orthopaedic conditions, as well as primary aural diseases and cases of feeding error. Of these 1,107 infants 240 had an aural infection on admission; in the remaining 867 the ears appeared normal when first seen but 191 later developed otitis media or mastoiditis—a total of 431 (39%) infants with ear disease. Of these, 268 recovered and 163 (38%) died. The following surgical procedures were carried out:

Bilateral myringotomies in 227 cases (109 died)
Unilateral ,, ,, 18 ,, (8 ,,)
Posterior drainage also ,, 64 ,, (48 ,,)

TABLE I.—*Relationship of Otitis Media to Parenteral Infections*

	Recovered	Died	Total
1. Respiratory:			
Bronchitis or pneumonia with otitis media or mastoiditis	60	43 (42%)	103
Bronchitis or pneumonia without complicating aural disease	168	*48 (22%)	216
2. Alimentary:			
Gastro-enteritis with otitis media or mastoiditis	118	75 (39%)	193
Gastro-enteritis without complicating aural disease	105	45 (30%)	150

* Of these 26 died within 24 hours of admission.

TABLE II.—*Results of Treatment of 431 Infants with Aural Disease*

Treatment	Recovered	Died	Total
Penicillin alone	32	14 (30%)	46
Chemotherapy alone	105	31 (23%)	136
Both penicillin and chemotherapy (extremely ill cases)	102	104 (50%)	206
No specific treatment (includes both mild infections and those dying within a few hours of admission before treatment had begun)	29	14 (33%)	43
Total	268	163 (38%)	43

These figures are striking in that they reveal the high incidence of otitis media in infants in hospital. Barrier-nursing technique was observed in all cases whether admitted to general wards or individual cubicles. The environment seemed to have no significant bearing on the subsequent development of the disease.

Prolonged clinical observation bears out the extreme difficulty of assessing whether otitis media is primary or secondary in cases in which respiratory or alimentary infections are also present.

CONCLUSIONS

On the question of treatment it is very difficult to draw specific conclusions, one can only generalize. There is no great difference between the results of those treated with myringotomy alone and those having posterior drainage; the mortality rate in both groups is high. Posterior drainage is performed by some surgeons only when symptoms persist after repeated myringotomies, whereas others consider that posterior drainage is indicated if there is no improvement after one adequate paracentesis.

Penicillin appears to have only a small place in the treatment of otitis media in young infants—possibly because of lack of sensitivity of the infecting organism. The mortality rate is high in spite of treatment with sulphonamides, penicillin, and intravenous fluids to combat dehydration.

Thanks are due to Dr. W. E. Crosbie, medical superintendent, Alder Hey Children's Hospital, for permission to publish these figures, to Professor Norman B. Capon for his kind interest and advice, and to Dr. Margaret Rogerson for assistance.

R. DERHAM, M.B., D.C.H.,
Deputy Medical Superintendent,
Alder Hey Children's Hospital.

Reviews

GYNAECOLOGY REFRESHER

Obstetrics and Gynaecology. A Revision Course for Practitioners. By C. Scott Russell, M.B., F.R.C.S.Ed., M.R.C.O.G. With foreword by J. Chassar Moir, D.M., F.R.C.S.Ed., F.R.C.O.G. Oxford Medical Publications. (Pp. 214; 21 figures. 12s. 6d.) London: Geoffrey Cumberlege (Oxford University Press). 1947.

The author has written this book for medical men returning to civilian practice who want to revise obstetrics and gynaecology and for any others who wish to refresh their memory. It is a small volume, just large enough to slip into the pocket, yet it contains an extraordinary amount of practical and useful information covering the whole of obstetrics and as much gynaecology as the practitioner is likely to need in his everyday work. On almost every page there is evidence that the author, far from repeating merely secondhand opinions, is himself a close observer, able to transform his observations into practical conclusions and to convey these conclusions to the reader in clear and convincing form. We like the advice given in discussing the management of the second stage of labour: "In all cases the foetal heart should be listened to carefully during the half hour following the rupture of the membranes, as one of the signs of cord prolapse may be a failure of the heart rate to pick up between pains." We like too the use of the radio in uterine inertia to keep the patient cheerful, but are less sure about the value of applying the forceps in constriction ring.

Though the author has done his work well, it must be said that obstetrics is not an easy subject to master. It requires much reading and long experience. It cannot therefore be expected that a small book such as this will equip the practitioner for the practice of midwifery, and it will probably be best read in conjunction with and as a supplement to some longer textbook. If this is done it will well repay careful study. As Prof. Chassar Moir says in the foreword, "It will stimulate an interest and will encourage the reader to a fuller study of the subject."

F. J. BROWNE.

HESS IN BRITAIN

The Case of Rudolf Hess. A Problem in Diagnosis and Forensic Medicine. Edited by J. R. Rees, M.D., F.R.C.P. (Pp. 224. 12s. 6d.) London: William Heinemann. 1947.

The main problem presented by this book is whether or not Hess was suffering from a paranoid schizophrenia during his stay in England. The authors conclude, though with reserve, that he probably was. The case is obscured by evidence of a psychopathic personality and by the repeated occurrence and remission—most dramatically during his trial—of a hysterical amnesia. In this account the authors consider these side-issues to a disproportionate extent and do not adequately discuss the more fundamental question of diagnosis.

Hess flew to England on May 10, 1941, apparently quite impulsively, on the conviction that he personally had only to say a few words to the King for peace to be declared. As soon as May 22 he was saying that he was surrounded by Secret Service agents who would drive him to commit suicide or poison his food. The systematized paranoia so begun persisted ever since. Early on he believed that doors were opened and shut and motor-cycles kept running to prey on his nerves. He would not eat unless others sampled the food. From time to time he would say he could not concentrate, that his mind went blank. An interview with Lord Simon revealed that the reason given for his flight had no basis in fact. Thereafter he was worse. All the people around him were under an evil influence, hypnotic or chemical, unconscious agents in a conspiracy to destroy him. In the early hours of July 15 he dashed suddenly along a corridor, "his face one of extreme despair, his eyes staring," and flung himself over a second-floor banister, breaking his leg. After that shifts of nurses watched him day and night, but he was still regarded as "not medico-legally insane."

In July, 1941, he came under the care of a psychiatrist with mental-hospital experience and was regarded as a characteristic mental-hospital inmate. He would lie with his fingers in his ears, smiling to himself, and when questioned would reply, "I am thinking." He hoarded odd bits of paper about the room and under the couch. In subsequent years, apart from the coming and going of amnesic states, he changed little. Auditory hallucinations were observed. He made a second attempt at suicide by plunging a bread-knife into his breast. In February, 1945, he handed in a medley of names of august personages and personal attendants under the hypnotic influence of the Jews. In October, 1945, he was transferred to Nuremberg gaol. He took with him a statement meant to be the basis of his case, a farrago of delusional material without relevance to legal or political issues. In it he says that the eyes of the people around him had a glassy look and changed from time to time, the result of an abnormal mental condition caused by a secret chemical; his food was contaminated by secretion from camels' and pigs' glands; his dictionary decayed when he touched it; his apples were injected with "hot poison." In Nuremberg gaol primary delusions were still appearing: "I will look at a piece of bread, and suddenly I feel sure it has been poisoned." Schizophrenic ambivalence was shown: asked for his signature, he would write it and immediately scratch it out, this performance being repeated several times. Nevertheless the medical commissions found him not insane but fit to plead, and the Russian physicians state a definite opinion that he was simulating and that his past paranoid illness was psychogenic. He was, however, then in an amnesic state, and the delusions had for the time receded, though they were to recur.

Hess's illness, therefore, is a chronic paranoid condition, progressive and without tendency to remission. It thus bears no resemblance to a purely psychogenic state. Hardly one of the most characteristic schizophrenic symptoms is lacking: primary delusions, systematization of delusions of a highly bizarre type, hallucinations in a clear state of consciousness, thought disorder and incoherence, affective impoverishment, and ambivalence and other gross disturbances of volition.

This analysis, when contrasted with that provided in the book, throws into relief the differences between two schools of psychiatry. Considered in the terms of a psychotherapeutic discipline, Hess's case was one of great difficulty and obscurity. Considered in the terms of a classical psychiatry, it was unambiguously schizophrenic from the beginning. The reason for the authors' doubts and hesitations is to be found in the inadequate theory by which, in common with others of their school, they were bound. They state (p. 212) that they attach relatively small importance to "diagnostic labels." In this they throw overboard a whole field of psychiatric knowledge. The making of a diagnosis of schizophrenia is not a bagatelle, but is fraught with consequences of a prognostic, therapeutic, and medico-legal kind. It was a fateful circumstance for Hess that a diagnosis of schizophrenia was reached only after several years, and after his trial was over.

ELIOT SLATER.

BASAL GANGLIA

Diseases of the Basal Ganglia and Subthalamic Nuclei. By D. Denny-Brown, M.D., Dr.Phil., F.R.C.P. Edited by Henry A. Christian, M.D., Sc.D., F.A.C.P., F.R.C.P.(Can.). (Pp. 45. 12s. 6d.) New York and London: Geoffrey Cumberlege (Oxford University Press).

This book, published as a separate monograph, is a chapter written by Prof. Denny-Brown for the *Oxford Loose-leaf Medicine*. In the earlier and more important part he has reviewed the literature on the diseases of the basal ganglia with reasoned criticism and much selection against the background of the anatomy and physiological activity of the basal grey matter.

Prof. Denny-Brown strives to show the relation of the extra-pyramidal system to that of the pyramidal, cerebellar, and sensory systems in the control of voluntary movement, and then to demonstrate in the various syndromes which he has discussed the deprivation of function caused by the lesion, and the significance of the residue. This is an admirable work of reference and a clinical exposition in the best tradition.

DENIS WILLIAMS.

TRAINING AFRICAN NURSES

African Medical Handbook. An outline of medicine and hospital practice for African nurses, orderlies and medical assistants. By Michael Gelfand, M.B., M.R.C.P. (Pp. 206; 22 figures. 15s.) Capetown: The African Bookman. P.O.Box 3115.

One of the greatest medical problems of the day is how to provide medical treatment for the vast undeveloped areas of Africa. There are far too few European doctors and in many cases they cannot understand the languages of the peoples with whom they have to deal. African doctors also are lacking. Apart from inadequate facilities for medical teaching there are as yet far too few people with the requisite secondary education to enable them to benefit from Western medical training. In this dilemma an answer has been found in the provision of African dressers, nursing orderlies, and medical assistants, who in many countries have already been placed in charge of important dispensaries. Textbooks are obviously required for the teaching of the African subordinate medical and nursing staff, but although a beginning has been made in Uganda and the Belgian Congo the supply is insufficient. The writing of such books is by no means easy: they must be written clearly and simply, for many Africans have only small knowledge of English; they must be absolutely accurate, for the African still firmly believes in the infallibility of the printed word; and finally they must tell exactly what the African must and must not do in all the emergencies with which he may be called upon to deal.

Dr. Gelfand comes out of the first test with flying colours. On the second count there is less certainty, for there are many minor inaccuracies. No one can diagnose sickling of red cells by placing a drop of blood on a slide and covering it with a cover-glass however long he leaves it (p. 166) unless he rings the cover-glass with vaseline. Red blood cells will not be found in the urine in blackwater fever (p. 193). Blackwater fever occurs more frequently in children than in adults in West Africa (p. 77). Many of the names of diseases used are no longer current—for example, "Malta fever," "catarrhal jaundice," and "climatic bubo"; while the constant use of "M. and B. drugs" as a synonym for sulphonamides is to be deprecated. Infective hepatitis is the name of a specific disease (p. 195). These, however, are minor blemishes which can be removed when a second edition is called for.

The author is at his best in describing treatment in detail from his extensive knowledge of work in a large African hospital, and the instructions in most cases are clear and concise. Some readers, however, would look askance at treating early cases of Gambian sleeping sickness with tryparsamide alone. There is no mention of the use of penicillin in the treatment of tropical ulcer, and curiously enough no mention at all of such a common disease as influenza or influenzal pneumonia, though he refers to such rare complaints as mumps encephalitis and to asbestosis. In many parts of Africa carbon tetrachloride has been given up in favour of the much less toxic carbon tetrachloroethylene. A special word of praise must be given to the numerous line drawings by Mr. H. H. D. Simmonds; these will do much to lighten the African's task in grasping the main facts of the cause and cure of common diseases.

G. M. FINDLAY.

The Collected Papers of the Mayo Clinic and the Mayo Foundation, Vol. XXXVIII, 1946, edited by Dr. Richard M. Hewitt and others (W. B. Saunders, 63s.), fall into certain broad groups. There are the hardy annuals such as peptic ulcer, cancer, and peripheral vascular disease, on which there is always something, if nothing fresh, to say. Then there are the Mayo Clinic contributions to recently described or rediscovered syndromes, such as Meig's syndrome, cystic fibrosis of the pancreas, or diffuse amyloidosis with macroglossia, in which a few i's are dotted and a few t's crossed. More useful are the reviews of series of cases—e.g., a study of 31 cases of primary carcinoma of the liver or the review of 83 proved cases of multiple myeloma. Finally there are the papers on subjects which workers at the Mayo Clinic have made their own, such as the group of papers on streptomycin or Allen's report on treatment with dicoumarol. Though there is nothing exciting in these 900 pages, they are nevertheless a fair summary of recent advances in routine hospital work. Few of us would choose this as preferred reading, but few of us, again, would not find much of interest and profit if this were the only book in the house on a wet week-end.

BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

Disputed Paternity Proceedings. By S. B. Schatkin. 2nd ed. (Pp. 614. No price.) New York: Banks and Company. 1947.

A general account of the medical and legal aspects.

Clinical Ophthalmology. By H. M. Traquair, M.D., F.R.C.S.Ed. (Pp. 264. 25s.) London: Henry Kimpton. 1948.

An introduction to ophthalmology for general practitioners and students.

The Social Sciences. A case for their greater use. (Pp. 46. 1s. 6d.) Prepared by the Social Science Committee of the Association of Scientific Workers, London.

A pamphlet advocating the greater use of the social sciences.

Transactions of the Medical Society of London. Vol. 64. Edited by W. E. Tanner, M.S., F.R.C.S. (Pp. 384. No price.) London: Harrison and Sons.

Papers on a wide variety of topics presented during 1944–6.

Practical Food Inspection. By C. R. A. Martin. Vol. 2. 3rd ed. (Pp. 284. 18s.) London: H. K. Lewis. 1948.

The inspection of food other than meat from animals killed in slaughterhouses.

Oxford Essays on Psychology. By William Brown, D.M., D.Sc., F.R.C.P. (Pp. 148. 10s. 6d.) London: William Heinemann. 1948.

Lectures on general psychology delivered to students.

Modern Psychiatry in Practice. By W. Lindesay Neustatter, B.Sc., M.D., M.R.C.P. 2nd ed. (Pp. 275. 12s. 6d.) London: J. and A. Churchill. 1948.

A general introduction to the practice of psychiatry for student and practitioner.

The Universe in the Making. By J. E. R. McDonagh, F.R.C.S. (Pp. 174. 7s. 6d.) London: Chaterson. 1948.

A medical man's personal account of the universe.

Basic Facts of Health Education. By W. P. Kennedy, Ph.D., L.R.C.P., F.R.S.Ed., *et al.* (Pp. 193. 7s. 6d.) London: The Pharmaceutical Press. 1947.

A collection of short articles for pharmacists.

Voluntary Social Services since 1918. By Henry A. Mess *et al.* (Pp. 255. 21s.) London: Kegan Paul, Trench, Trubner. 1948.

A review of the social services in Britain.

Harmony of Nature. By L. Richmond Wheeler. (Pp. 200. 10s. 6d.) London: Edward Arnold. 1947.

The author, a biologist, elaborates his theory of "co-operation for existence" in nature.

The Psychology of Diet and Nutrition. By L. S. Selling, M.D., and M. A. S. Ferraro, M.S. (Pp. 192. 8s. 6d.) London: John Lane, The Bodley Head. 1947.

A simple account by a dietitian and a psychiatrist intended for dietitians and housewives.

Tuberculosis in the Commonwealth, 1947. (Pp. 328. 15s.) London: Pendragon. 1947.

The transactions of the Commonwealth and Empire Tuberculosis Conference convened by the N.A.P.T. in 1947.

Psychiatry: a Short Treatise. By W. A. O'Connor, L.M.S.S.A., D.P.M. (Pp. 380. 35s.) Bristol: John Wright. 1948.

A general introduction to psychiatry.

An Outline of the Development of Science. By Mansel Davies. (Pp. 214. 3s. 6d.) London: Watts (Thinker's Library). 1947.

A short history, with illustrations.

Clinical Endocrinology and Constitutional Medicine. By A. P. Cawadias, O.B.E., M.D., F.R.C.P. (Pp. 362. 42s.) London: Frederick Muller. 1947.

The author stresses the clinical aspects of endocrinology and includes a number of illustrations.

Nova et Vetera

THE AMERICAN SYDENHAM

During the present century general historians in America have begun to turn their attention towards Benjamin Rush, of Philadelphia, and have dealt with his contributions to social reform and to education. Although Rush was never a major political figure he belonged to a group of versatile individuals who helped to bring about the independence of the United States. One of the five medical men who signed the Declaration of Independence, he was also a member of the Constitutional Congress and was for many years Treasurer of the U.S. Mint. Nevertheless, as a national figure Rush has been overshadowed by such men as John Adams, Thomas Jefferson, Benjamin Thompson, and that other embodiment of eighteenth-century versatility, Benjamin Franklin. Rush, however, has never been neglected by the members of his own profession, and his position as the leading medical man of his time has not been challenged. He has been hailed as the American Sydenham and as the Father of American Psychiatry. Papers read at a special meeting of the College of Physicians of Philadelphia, held on Nov. 6, 1946, to commemorate the 200th anniversary of the birth of Rush, who was one of the founders of the College, have now been printed,[1] and these provide a valuable supplement to the full-length life by Dr. Nathan Goodman published in 1934.

The first paper in this symposium is by Dr. R. H. Shryock, who refers to the wide divergence of views concerning Rush held both by his contemporaries and by present-day writers. These range from John Coakley Lettsom's claim that Rush combined judgment and sagacity "in almost unprecedented degree" to Elisha Bartlett's acid observation that there was more "utter nonsense and unqualified absurdity" in Rush's works than in the whole compass of medical literature. According to some critics Rush's voluminous *Medical Inquiries and Observations* contain nothing of value and only serve to show how easy it is for a facile writer to build up an unmerited reputation; others regard his writings as a mine of valuable clinical records and as containing many forecasts of modern views.

Rush was of English Quaker descent, and was born in Byberry Township, Philadelphia County, in 1745. After taking his B.A. degree at Princeton in 1760 he was apprenticed for six years to Dr. John Redman, of Philadelphia. He attended the first course of lectures on anatomy given in 1762 by Dr. William Shippen the younger, a pupil of the Hunters and the friend of John Fothergill. Like so many of his compatriots Rush came to Edinburgh, where he took his M.D. in 1768, and he then studied in London and Paris. On his return to America in 1769 he was elected professor of chemistry in the College of Philadelphia. His appointment completed the medical faculty of the first medical school established in what is now the United States. In 1789 he succeeded John Morgan as professor of the theory and practice of medicine in the College of Philadelphia, and when in 1791 the University of Pennsylvania was founded Rush was appointed professor of the institutes of medicine and of clinical medicine. In 1796 he received the additional appointment of professor of the practice of physic, and he also acted as physician to the Pennsylvania Hospital. During the revolutionary war he was physician-general to the military hospitals of the Middle Department of the United States Army. He died in 1813.

Dr. Shryock deals at length with Rush's theory of pathology. The prevailing medical teaching of his day was that of Cullen, according to which diseases were minutely classified and every disease was supposed to possess an appropriate specific treatment. Rush rejected the nosological arrangement of diseases and expounded a modified form of brunonianism. He claimed that all fevers resulted from (1) a predisposing debility, (2) a stimulus which was the immediate inciting cause, operating upon a debilitated body to produce (3) a convulsive excitement or excessive action in the walls of the blood vessels. Subsequently he declared this "convulsive action" to be the underlying feature of all apparently distinct forms of illness. Dr. Shryock points out that in certain respects Rush's views no longer seem so strange to medical thinking as they did to his contemporaries and immediate successors. "Predisposing debility" was analogous to the modern idea of lowered resistance. Stimulus (the immediate exciting cause) was conceived broadly enough to include anything which would be listed to-day as an external aetiological factor.

Rush was certainly the ablest American clinician of his time. He described cholera infantum (1773) and gave one of the earliest accounts of dengue (1780). He wrote a valuable pamphlet on the hygiene of troops (1797), and his accounts of the North American Indians (1774 and 1778) and of the German inhabitants of Pennsylvania are among the earliest American contributions to anthropology. The original bent of his mind is shown in his inquiries into the effects of alcohol on the mind, into focal sepsis, and into the use of arsenic in cancer. His *Medical Inquiries and Observations upon the Diseases of the Mind* (1812) is the earliest systematic American treatise on the subject. One of Rush's most famous writings is his account of the Philadelphia epidemic of yellow fever in 1793. Rush took a leading part in fighting this epidemic, and incurred the hatred of his fellow citizens by proclaiming that the fever was the result of filth in the streets and not an importation. His treatment consisted mainly in venesection and purgation, low temperature in the sick-room, and the application of cold water both within and without. He gave purgatives in enormous doses—a powder of 10 gr. of calomel and 15 gr. of jalap administered not once but repeatedly. As a blood-letter Rush was a veritable Sangrado. He did not hesitate to remove a quart at a time and to repeat this procedure two or three times within forty-eight or seventy-two hours. "Bleeding," he wrote, "should be repeated while the symptoms which first indicated it continue, should it be until four-fifths of the blood contained in the body are drawn away." Rush claimed that many more patients with yellow fever recovered under his treatment than under the older use of wine, blisters, and bark. Dr. Philip Syng Physick ascribed his own recovery from yellow fever to his treatment by Rush with the removal of 76 oz. of blood by 22 bleedings in ten days. Rush's claims were hotly contested by William Cobbett and by many of his medical colleagues.

In the second paper in this symposium Prof. O. H. Perry Pepper deals with "Benjamin Rush's theories on blood-letting after one hundred and fifty years." Rush found indications for bleeding not only in the pulse but also in the appearance of the blood in the bleeding-bowl. He was especially impressed by blood covered with a buffy coat. This blood was termed "sizy," and the more sizy the blood the more clear the indication for bleeding, according to Rush. Prof. Pepper points out that Rush was partly right in using the thickness of the size as an indication of the presence of an inflammatory process, and he gives an interesting account of the growth of knowledge concerning the significance of the sedimentation rate. What Rush did not know was that anaemia of itself increased the sedimentation rate and, of course, the siziness of the blood. Each blood-letting therefore paved the way for another, for each removal of blood made the patient more and more anaemic.

Appended to these two lectures is a list of "Benjamin Rush's apprenticed students," taken by Mr. James E. Gibson from a notebook in the Rush Manuscript Collection in the Ridgeway Library, Philadelphia. This list contains the names of 135 apprentices who lived with the Rush family and in near-by lodgings between 1770 and 1812. Rush selected his apprentices with care; the majority were the sons of personal friends or were recommended by his old students. In 1776 each pupil paid a fee of 100 guineas.

Wellcome Historical Medical Libary. W. J. BISHOP.

[1] *Trans. Stud. Coll. Phys. Phila.*, 1946, **14**, 113, 121, 127.

The Royal College of Nursing will hold a conference from May 31 to June 2 in order to discuss design, equipment, and administration. Tickets in the first place will be allocated through the branches and sections of the College and through affiliated associations. Any remaining tickets, for which the fee is one guinea, may be obtained on application to the Conference Secretary, Royal College of Nursing, Henrietta Place, Cavendish Square, London, W.1.

BRITISH MEDICAL JOURNAL

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YES AND NO

The result of the fourth plebiscite to be held by the British Medical Association will be known soon after this issue of the *Journal* is published. If the majority of consultants and specialists, general practitioners, and those working whole-time in voluntary hospitals vote against accepting service, and if this majority includes approximately 13,000 general practitioners, the B.M.A. will continue to advise the medical profession not to enter the National Health Service on July 5. The corollary of this is that if the majority as stated is not secured the B.M.A. will not offer this advice. Should the majority be in favour of accepting service in view of the changed situation resulting from Mr. Bevan's concessions, the Representative Body may consider it wise to urge the minority to enter the new Service so that the majority may have a fair chance of giving the public at least some of the benefits that have been so extravagantly promised it. The facilities for a comprehensive medical service for all will not be available on July 5, and a disappointed public will look for a scapegoat. There will probably be some men who on grounds of conscience will not enter a State medical service. They demand the respect always accorded in this country to the objector who is conscientious. If as a profession we behave with dignity and show tolerance to those who differ we shall avoid the bitterness attending the introduction of the National Health Insurance Act of 1911. If as medical men and women we fall out among ourselves we shall lose the strength of unity which was so dramatically demonstrated when Mr. Bevan's intransigence provoked an overwhelming vote of no confidence in the National Health Service Act in the form in which it was before the profession in January of this year. Mr. Bevan and the Government were compelled by the plebiscite of February to introduce an Amending Act which in December last Mr. Bevan refused even to contemplate. We believe that this is the first time any section of the community has been successful in persuading the Government to modify an Act already on the Statute Book, an Act, moreover, endorsed by a Parliamentary majority in the ill-starred and unprecedented debate in the House of Commons on Feb. 9.

The plebiscite of February taught us one thing, and that is that when medical men and women are convinced that their professional and intellectual freedom is threatened they can unite to good effect. If the present plebiscite does not produce a result similar to that held in February it may be argued that conviction is now lacking. That Mr. Bevan has made concessions was acknowledged by Dr. H. Guy Dain, the Chairman of Council, in a letter published in last week's *Journal*. The B.M.A. Council considered that these concessions had not sufficiently safeguarded the freedoms of the profession. Public opinion, a powerful force not to be lightly disregarded, inclines to the opposite point of view. This opposite point of view is shared by many responsible medical men whose opinions command respect. For example, at a meeting held by consultants in B.M.A. House last week, an account of which appears elsewhere, Sir Reginald Watson-Jones, who had openly declared his opposition to the Act before the Minister had made his concessions, advised those present to accept service in view of the changed situation.

It is possible that the present plebiscite will show an almost equal division of opinion on whether or not to enter the Service. If this happens the medical profession will be in a dilemma. In that event we shall be faced with the paradox that when Mr. Bevan tried by opposition to split the profession he failed, and that now by making concessions in a conciliatory manner he has succeeded in dividing us. If approximately half those who vote are prepared to enter the Service, then Mr. Bevan may well believe that he has enough medical men with which to operate it on July 5. But neither Mr. Bevan, nor the medical profession, nor the British public will be able to look upon this situation with anything but dismay. At all costs we must strive to preserve our unity and agree to differ, if differ we must, in a spirit of tolerance. The forces that bind medical men together are much stronger than those that tend to separate them. We must, too, remind ourselves that the B.M.A. has declared its "whole-hearted desire" for a comprehensive medical service available to everyone in Britain. The Representative Body voted in favour of "the 100% issue." These two things added together mean a national medical service. What matters to the medical man working in this service is his freedom to apply the art and science of Medicine according to his training and his conscience, and his freedom to express his opinion by voice and pen on all aspects of professional life, including the administration of the service in which he works. We have always held that these freedoms and free choice of doctor could not be maintained in a full-salaried State medical service. The promised Amending Act would seem to be a sufficient safeguard against the introduction of a full-salaried service under the National Health Service Acts of 1946 and 1947. Mr. Bevan has agreed to include in the terms of contract his assurance that freedom of opinion on all aspects of professional life will be safeguarded. Those who think these are not sufficient must determine "as reasonable people"—to quote Dr. Dain's words—what other safeguards are necessary and endeavour to obtain them. The Edinburgh Division of the B.M.A. on Sunday reminded us, too, of the need for "warning the public that the full range of service will not be available for many years to come." On this point the public has been misled by ill-informed publicists, and it will need repeated correction.

THE MEGALOBLASTIC ANAEMIAS

In no branch of medicine has factual knowledge accumulated more rapidly in recent years than on the subject of the anaemias. This has been accompanied by a reorientation of ideas, preoccupation with cytology having been replaced by an interest in metabolic, chemical, and nutritional factors underlying haemopoiesis. The initial stimulus was provided by Minot and Murphy's[1] demonstration that patients with Addisonian pernicious anaemia could be restored to health by the addition of liver to their diets. Peabody had already shown that in this disorder there was a proliferation of primitive erythroblasts in the bone-marrow and that this megaloblastic hyperplasia gave place to a normoblastic haemopoiesis when remission occurred. Sternal puncture has demonstrated that there is a group of anaemias to which this megaloblastic change in the bone-marrow is common.

Although the megaloblast has long provided haematologists with material for acrimonious argument, the appearance of megaloblastic hyperplasia is so typical that it can be recognized by the tyro. All agree on the appearances, but interpretation is still debated. Peabody suggested that an arrest of maturation was the underlying fault, and owing to the confusion caused by the varied meanings imputed to the term megaloblast it was for long believed that the cells of the bone-marrow in pernicious anaemia were erythroblasts of an immature type which existed in normal marrow in scanty numbers. It is now generally accepted that the megaloblast is a pathological erythroblast which is seen, with rare exceptions, only in the marrow of patients with the anaemias now under discussion. "Maturation arrest" cannot describe this change because such cells do not represent a stage in normal maturation. It is still uncertain whether the reversion to normoblastic erythropoiesis which accompanies remission entails a rapid maturation of megaloblasts to form megalocytes, or whether a megaloblast can be transformed into a normoblast of the same maturity. Confusion has been increased recently by claims to recognize cells intermediate between normoblasts and megaloblasts, and if their existence is accepted such transformation must be granted. Mallarmé[2] has called the megaloblast a normoblast suffering from a nutritional deficiency, and it may be that grades of deficiency exist.

The anaemias which share this characteristic bone-marrow change may be spoken of, as Davidson and Davis[3] have suggested, as the megaloblastic anaemias. The main members of the group are Addisonian pernicious anaemia, pernicious anaemia of *Diphyllobothrium latum* infestation, pernicious anaemia of pregnancy, nutritional megalocytic anaemia, the megaloblastic anaemias of infancy and childhood, the megaloblastic anaemia accompanying steatorrhoea, and certain refractory megalocytic anaemias. It is rational to seek for these various disorders a common cause, and Castle's hypothesis seemed to provide this. However, difficulties arose when it was found that different members of the group responded differently to treatment with liver preparations, which *ex hypothesi* should have been fully effective in all. The preparations generally in use can be classed as refined extracts for injection, crude extracts for injection, and proteolysed liver for administration by mouth. Addisonian pernicious anaemia and that due to the broad tapeworm respond adequately to all of these. Pernicious anaemia differs from others of the group in its association with degeneration of nervous tissues, from which danger adequate dosage with liver protects the patient. Von Bonsdorff[4] has suggested that pernicious tapeworm anaemia is due to the inhibition of the interaction of the intrinsic and extrinsic factors, which occurs only when the worm is sufficiently high in the intestine. In the other anaemias of this type response to refined liver extracts is absent or indifferent. Crude extracts are effective in some, while in others proteolysed liver is apparently the only useful preparation. In this group Davidson[5] would place idiopathic refractory megaloblastic anaemia, which appears to be the condition described by Israels and Wilkinson as achrestic anaemia. Watson and Castle[6] have been able to separate two varieties of nutritional megaloblastic anaemia, one responding to refined extracts and the other to crude extracts or yeast.

Matters had reached this degree of confusion and complexity when the discovery of folic acid was announced. The steps which led to the isolation and later to the synthesis of this substance are recounted in Dr. J. F. Wilkinson's papers, the second of which appears in this number of the *Journal*. He and others have shown that it is effective in all forms of megaloblastosis of the bone-marrow. How completely efficacious it may be is not yet agreed, because there is some evidence that satisfactory blood levels are not always maintained. In the steatorrhoeas, in which a mixed megaloblastic–normoblastic hyperplasia is common, he finds it effective in proportion to the degree of megaloblastosis. The problem has now become how to fit folic acid into the aetiological puzzle. Since all megaloblastic marrows become normoblastic under the influence of folic acid it seems likely that this substance is itself the essential missing factor. Refined liver extracts, effective in pernicious anaemia, are virtually devoid of folic acid, and Davidson[5] has suggested that they act by liberating folic acid from the inert conjugated form in which it exists in the diet. The other megaloblastic anaemias he regards as due to a failure of supply of conjugated folic acid, since purified liver extract is ineffective in them. A paper by Prof. Davidson and others, describing the successful treatment with folic acid of three cases of pernicious anaemia of pregnancy which did not respond to injections of liver extract, appears elsewhere in this issue. Davidson's hypothesis does not fully explain the failure of folic acid treatment in some cases, nor the persistence of megalocytosis noted by Wilkinson, and he suggests a third factor may be present in proteolysed liver. Jacobson's[7] observation that when folic acid is incubated with xanthopterase its haemopoietic activity is greatly increased indicates that the final solution may be more complicated. The most recent development in this field is the preparation of red pigments

[1] *J. Amer. med. Ass.*, 1926, **87**, 470.
[2] *Blood*, 1948, **3**, 103.
[3] *Advances in Internal Medicine*, 1947, **2**, 481.
[4] *Blood*, 1948, **3**, 91.
[5] *Blood*, 1948, **3**, 107.
[6] *Amer. J. med. Sci.*, 1946, **211**, 513.
[7] Communication to International Physiological Congress, Oxford, 1947.
[8] Smith, E. Lester. *Nature, Lond.*, 1948, **161**, 638.
[9] *Blood*, 1948, **3**, 68.

(described as differing forms of the classical liver factor) from ox liver or proteolysed liver extracts which are reported to be effective in cases of pernicious anaemia and subacute combined degeneration in doses equivalent to some 20 μg. daily (possibly only 2.5 μg.).[8]

In pernicious anaemia folic acid has a greater theoretical than practical importance. Like others, Wilkinson has found that while controlling the anaemia it has no effect on the subacute combined degeneration of the cord. There are several reports which suggest that it increases the rapidity of onset of nervous symptoms. Ross, Belding, and Paegel[9] consider that it may interfere with the metabolism of l (+) glutamic acid in the nervous system. Whatever the explanation, folic acid is a dangerous drug in pernicious anaemia, and the treatment of choice remains the injection of a potent liver extract. The place for folic acid is in the treatment of the other megaloblastic anaemias, which are often refractory to liver and in which changes in the nervous system do not occur.

THE NEW "B.P."

The publication, with effect from September next, of another *British Pharmacopoeia* is a noteworthy event. The new issue is the seventh of its series to appear under the auspices of the General Medical Council. The first was published in 1864 and the sixth in 1932. In normal times an interval of ten years is considered reasonable; the prolongation to the sixteen years separating the current and the forthcoming issues is due to war and post-war restrictions and frustrations. The issue of seven Addenda, six of them in wartime, has bridged the interval.

For the origin of the *Pharmacopoeia* it is necessary to go back to the reign of James I. The Royal College of Physicians of London issued the first *London Pharmacopoeia* in 1618; similar publications made their appearance in Edinburgh in 1699 and in Dublin in 1807, and all three continued through various editions down to the middle of the nineteenth century. The preparations contained in these three formularies, however, were not all uniform in strength, and in view of the confusions which arose occasion was taken in the Medical Act, 1858, which set up the General Medical Council, to ordain that the Council should publish under its direction "a Book containing a list of medicines and compounds, and the manner of preparing them, together with the true weights and measures by which they are to be prepared and mixed, and containing such other matter and things relating thereto as the General Medical Council shall think fit. . . ."

The new volume in its familiar red cover bearing the royal coat of arms and announcing itself as issued "by authority" (complete in every respect except the price, which has yet to be fixed by the Treasury) is larger than its predecessor, running to not far short of a thousand pages. The Pharmacopoeia Commission, which has carried through the long and arduous work of preparation, is a body consisting of ten members under the chairmanship of Prof. J. A. Gunn. Three of the members, including Prof. Gunn, were on the Commission which prepared the *B.P.* 1932, and the secretary, Dr. C. H. Hampshire, has acted in that capacity for both issues. The task has been more laborious and exacting than has attended any previous issue, not excepting even the first, but the Commission has been assisted by many experts and counsellors, including a clinical committee of over twenty members, and eight other committees, some of them with several subcommittees. In a preface to the work the Pharmacopoeia Committee of the G.M.C., which has undertaken a general supervision, pays a high tribute to the Commission for its unsparing efforts to bring the publication up to the utmost possible level of completeness and accuracy.

The task of those engaged in compiling the *Pharmacopoeia* is continuous. The ink is hardly dry upon one publication before the work on the next is begun. The publication therefore cannot be, and never aspires to be, up to date. The vast amount of experiment in devising suitable formulae and assessing the value of new preparations forbids. The use of pharmaceutical products by the medical profession is subject to constant change. It is not only ephemeral preparations which have their day and cease to be, but drugs of high reputation and dependability have their periods of popularity and decline. New drugs make their appearance and are for a time acclaimed, and then experience shows that they do not quite fulfil expectations, and they recede into the background or are superseded by some preparation for which similar or greater claims are made. The enterprise of pharmacists, the experiments of laboratory workers, the eagerness of clinicians present a situation which, excellent as it is from the point of view of medical and pharmaceutical progress, offers obvious difficulties to the compilers of an official and authoritative publication who have to look, not to the immediate summer, but to five or ten years ahead. It may well happen that when a new *Pharmacopoeia* is published some preparation may be on the crest of its wave of usefulness and finds no mention at all, while another which has been virtually discarded may be the subject of the usual monographs.

The changes introduced into the new *Pharmacopoeia* are not so many as might be expected in view of the great progress which has taken place in the laboratories, but it must be remembered that the comparison is not with the 1932 issue but with that issue together with, and as modified by, the several Addenda subsequently brought out, the last of which appeared in 1945. Ever since a Colonial and Indian Addendum was issued at the beginning of this century an endeavour has been made to ensure that the *Pharmacopoeia* shall be suitable for the whole of the British Commonwealth; but only preparations in general use throughout the Empire are included, not the various substances which have had but a local favour.

It would be an interesting exercise to take all the seven *Pharmacopoeias* and trace through them the enlarging history of modern pharmacy. Probably the most impressive thing which would appear as the result of such a review would be the large accessions of knowledge which have widened the boundaries of pharmaceutical science and the ever-increasing precision of testing and analysis. One has only to reflect upon the extensions in therapeutics which have followed the introduction of hormones, vaccines, sera, vitamins. In this latest *Pharmacopoeia*, for example, it has been necessary to enter upon an entire reassessment of

the value of the drugs which have appeared as a result of the developments in chemotherapy. With all this the definitions have continually become more exact and the tests more stringent; new instruments and methods have been introduced; and the standards by which a substance can be regarded as having an adequate therapeutic value have been raised. Some years ago the Fédération Internationale Pharmaceutique laid down a formidable list of subjects which should have a place in the studies of the pharmaceutical student. It included analytical and biological, physiological and pathological chemistry, chemical and galenical pharmacy, pharmacognosy, micrography, toxicology, microbiology, crystallography, and disinfection, and that did not exhaust the list, which ran on into general hygiene and public health legislation. Then from time to time, as new and authoritative *Pharmacopoeias* come forward, the pharmacist must readjust his knowledge and his practice, finding as he does that the composition and character of the drugs and galenicals to which he has been accustomed are affected by the requirements of the new issue which replace those of the old.

A complaint has been made against recent issues of the *Pharmacopoeia*—a complaint which may possibly be levelled against the new one—that they have been constructed not so much for the retail pharmacist as for the large manufacturing laboratory, since it is only the latter which has the resources to perform all the tests set out in 200 recondite pages of the appendix in the new issue. But that, of course, does not apply to the large numbers of injections, solutions, pills, ointments, and other articles and preparations which are the subject of a very large proportion of the monographs, and which are not beyond the capacity of any retail pharmacy properly equipped. One of the striking features of this new compilation is the introduction of as many as fifty-seven new injections; the current *B.P.* includes only half a dozen. In the earlier edition also there was only one tablet preparation (glyceryl trinitrate); in the 1948 edition eighteen tablet preparations are included. Another change is the elimination of all the fresh infusions, the prescription of which has continued to decline, and in the new issue the principle of preparing infusions from concentrated preparations is fully recognized.

One rises from a preliminary study of the new compilation with an increased respect—perhaps an increased sympathy—for the pharmacist, the practitioner's loyal and painstaking ally, and a renewed appreciation of the skill and care which invariably go to the testing of drugs and the dispensing of prescriptions.

CONGENITAL MEGACOLON

Into the colon from above there comes a constant flow of intestinal contents. If there is not a corresponding evacuation from below, these contents accumulate and the bowel must enlarge to contain them. Accumulation of faeces in a grossly dilated bowel occurs in two quite distinct conditions. In the first, seen typically in neglected children or those with congenital malformations of the anus, the bowel gives up the struggle and loses the reflex to empty itself which should be produced by distension. The resulting mass of faeces may be enormous, and semi-fluid matter may leak past it to produce a distressing overflow diarrhoea. The treatment, however, is simple and (given co-operation by those in charge of the child) satisfactory. In the second variety, on the contrary, the bowel is not indolent but makes violent efforts to evacuate its contents, efforts which are thwarted in some way or other which is far from being fully understood. The result is the picture described by Hirschsprung, with huge waves of visible peristalsis, vast discharges of gas and faeces at varying intervals, and a gross hypertrophy of the muscular wall of the bowel suggestively similar to that seen in the stomach behind a hypertrophic stenosis of the pylorus. This group can itself be subdivided into two distinct clinical types. In the first the stasis, though obstinate and distressing, is neither very dangerous nor intractable. It responds to a careful regimen, to excision of loops of bowel, to sympathectomy, and for some mysterious reason to the high spinal anaesthesia of which Prof. E. D. Telford and Mr. H. A. Haxton give such an encouraging account elsewhere in this issue. In the other type, however, all these methods of treatment fail. Affected children are pitiable creatures, grossly deformed by an enormous belly, passing from crisis to crisis of obstruction till a final one results in death. There must be some essential difference between the two categories, and a thorough comparison of *x*-ray and clinical observations should help to solve the problem. The work of Munro Cameron upon the absence of ganglia in low segments of the bowel in certain cases may provide a clue to the answer.

SEDIMENT IN THE STOMACH

An intricate study of the cytology of the gastric juice has recently been undertaken by Tomenius.[1] Early in his investigation he found that the sediment of resting juice obtained in the usual way was valueless for cytological study. Cells which reached the gastric juice, either by active diapedesis through the mucosa or by desquamation from the surface epithelium, were rapidly altered by the hydrochloric acid. Further damage was caused by the swallowed saliva or by regurgitation of the duodenal contents. As a result stained preparations consisted largely of amorphous material in which the remnants of cells could be identified with difficulty.

It was found that digestion of the cells by hydrochloric acid could be prevented by the administration of an isotonic solution of sodium bicarbonate by the continuous-drip process. To give this solution and to aspirate the saliva and prevent duodenal regurgitation Tomenius devised a stomach tube the lumen of which was divided into two. This tube reached only to the lower end of the oesophagus, and while saliva could be aspirated through one half isotonic sodium bicarbonate solution could be instilled through the other. In addition each division of the main tube contained a smaller tube. The first was a stomach tube for the recovery of the gastric contents, and the second extended to the duodenum so that continuous suction could be maintained and regurgitation prevented.

After preliminary investigation of the cells found in the saliva and the duodenal contents stained smears made from the material aspirated from the stomachs of normal individuals were studied. In these it was found that the sediment was scanty and cellular elements in it rare. Material was also obtained from 48 patients suffering from various complaints, including peptic ulceration, gastritis, carcinoma ventriculi, pernicious anaemia, and leukaemia. Normal smears were seen in cases of gastritis with achlorhydria,

[1] Tomenius, J. H., *Acta med. scand.*, Suppl., 1947, 189.
[2] Papanicolaou, G. N., *J. Amer. med. Ass.*, 1946, **131**, 372.

gastric and duodenal ulcers without gastritis, and carcinoma of the cardia or pylorus. Abnormal sediment was obtained from patients with gastritis where acid secretion was present, and with advanced carcinomas of the body of the stomach even when associated with achlorhydria. In all these cases leucocytes were greatly increased, and in the smears obtained from the patients with cancer many red cells were present. No neoplastic cells were seen, which is in contrast to the work of Papanicolaou.[2]

The investigation carried out by Tomenius is a model for its thoroughness and shows up the errors which are likely to occur when gastric sediment is obtained by less careful methods. The lessons to be learnt from it are, however, few. Gastritis is now diagnosed more frequently abroad than in this country, but much more experience with this painstaking procedure is required before the finding of an abnormal gastric sediment can be accepted as evidence of the existence of the condition.

THE TOXICITY OF AGENIZED FLOUR

The latest work in this country on agene-treated flour was described in an annotation recently in these columns.[1] Keen interest in the subject has also been shown in the U.S.A., where Sir Edward Mellanby's observation that agenized flour caused hysteria in dogs supplied the necessary clue to workers who had already suspected that certain processed wheat products were a frequent cause of this abnormality. In two extensive investigations they have now fully confirmed Mellanby's conclusions, and have made progress in a study on the effect of agenized flour upon other animals and upon the human subject.

At Chicago a team headed by Silver[2] gave dogs a diet which was adequate in proteins, vitamins, and other nutrients, but which contained 70% of the heavily agenized white flour. Neurological disorders developed within a week, with symptoms which varied in each animal but which usually included ataxia, weakness, and typical epileptiform fits. When electroencephalographs were recorded daily a cerebral dysrhythmia indistinguishable from that of human epilepsy appeared within 48–72 hours after the start of the agenized diet. Monkeys developed asynergy, weakness, and tremors, sometimes accompanied by cerebral dysrhythmia. In cats ataxia was the most prominent feature. An abnormal accumulation of reddish pigment, presumably a porphyrin, appeared around the head, eyes, and nose of rats fed on agenized whole-wheat flour. As observed in this country, the toxic agent was found to be formed from the protein of the wheat, particularly from the gliadin fraction, while casein and lactalbumin also became toxic when treated with agene. Intravenous infusions of mixtures of synthetic amino-acids which had been so treated caused seizures in dogs, but the only individual acids with this effect were cysteine and cystine. In the previous annotation reference was made to the work of Moran[3] in this country, who has also suggested that the toxic agent may be formed by the action of agene on amino-acids containing sulphur.

Elvehjem and his colleagues[4] at Madison have shown that unbleached wheat, irrespective of variety, does not cause hysteria in dogs. When agenized flour was included as 84% of the diet the times which elapsed before the appearance of hysteria varied according to the concentration of agene which had been used. Thus when 1 cwt. of flour was treated with 1 g. of agene fits occurred after 13–39 days, whereas with 20 g. of agene fits were observed after only 2–5 days. On the other hand when flour treated with 1.2 g. of agene per cwt., which is about the level used commercially, was given to dogs as 30% of their food, which represents about the proportion of flour in the average human diet in the U.S.A., they remained free from hysteria over a period of 12 weeks. In studies of the blood of affected animals no biochemical abnormalities could be detected. In agreement with previous findings improving agents other than agene (NCl_3) did not cause flour to become toxic. Agenized flour was found to retain its toxic properties even after storage for several months. Investigation of the various fractions of agenized flour gave further support to the view that the toxic agent is in the protein fraction, and not in the carbohydrate or lipoid fractions. No ill effects were observed when agenized flour was fed to rats, guinea-pigs, or chicks; cats had convulsive seizures, while monkeys developed abnormal electro-encephalographic patterns without obvious hysteria. In preliminary experiments on 5 human subjects, aged 6–16 years, wheat products treated with 3–20 g. of agene per cwt. were given in amounts of 70–105 g. daily for 2–4 weeks, but no electroencephalographic abnormalities or symptoms resembling hysteria were observed.

Official recognition of the danger of agene as an improver for flour may be implied from the publication of a letter from F. G. Boudreau, Chairman of the Food and Nutrition Board of the U.S.A. National Research Council, to Dr. P. B. Dunbar, Commissioner of Food and Drugs. Recommendations are made that research on the nature of the toxic agent and its effects should be intensified, that plans for industrial plant using chlorine and chlorine dioxide, or other "improvers," should be prepared, while in the meantime the use of agene should be reduced to the minimum necessary for the type of flour which has to be treated. More rigid restrictions are not at present contemplated, since it is considered that a too drastic interference with familiar baking practices might well aggravate the present food crisis.

ERYTHROBLASTOSIS AND KERNICTERUS

The problem of erythroblastosis foetalis continues to become more complex. The theory of Rh sensitivity as first outlined by Levine[1] has suffered so many modifications at the hands of the serologists that the facts of the matter have become dim owing to a mushroom growth of literature and a confused nomenclature. In the case of kernicterus, for example, it is now accepted that this encephalopathy results from incompatibility between an Rh-negative mother and an Rh-positive baby, with the consequent production of anti-Rh factors which pass from mother to foetus. Apart from the immediate risk to life, permanent damage to the central nervous system, causing spasticity, athetosis, or mental defect, is a frequent result of kernicterus, which is recognized morphologically by the staining of the basal nuclei of the brain with bile pigment, with a consequent degeneration of nerve cells.

A recent paper by Wiener and Brody[2] seems to show that the matter is not quite so straightforward as most clinicians had hoped. Aware of apparent discrepancies, they have investigated kernicterus from both the laboratory and clinical standpoint, and in so doing have arrived at a new conception of the disease. They conclude that the clinical manifestations of erythroblastosis depend upon the quality as well as the quantity of abnormal bodies in the maternal

[1] *British Medical Journal*, 1948, **1**, 350.
[2] *J. Amer. med. Ass.*, 1947, **135**, 757.
[3] *Nature, Lond.*, 1948, **161**, 126.
[4] *J. Amer. med. Ass.*, 1947, **135**, 760.

[1] *Amer. J. Obstet. Gynec.*, 1941, **42**, 925.
[2] *Amer. J. ment. Def.*, 1946, **51**, 1.
[3] *J. Pediat.*, 1946, **29**, 462.

serum; and that erythroblastosis foetalis comprises three rather than one major disease syndrome, depending on the type of antibody. These subdivisions are termed icterus gravis neonatorum, congenital haemolytic disease, and icterus praecox—the first two being of major importance. Icterus gravis neonatorum is thought to be due to bivalent antibodies (agglutinins) present in the maternal serum. Because of their size they are normally unable to pass through the placenta, but are "milked" into the foetal circulation by the uterine contractions at birth. The infant is normal at birth but develops jaundice and toxaemia shortly afterwards. In vessels where the circulation is sluggish agglutination takes place and thrombi form—the nature of the signs depending on the location of the latter. The liver is almost invariably affected. Erythroblastaemia is due to thrombi in the bone marrow, not necessarily accompanied by anaemia, and kernicterus is the outcome of a blockage of vessels in the brain. When similar symptoms occasionally occur as a result of univalent antibodies it may be because the infant is dehydrated, with consequent premature formation of X-protein and co-glutination. Other cases may rarely occur as a result of AB or Hr sensitization. Transfusion is useless in this group.

The second group—congenital haemolytic disease—is, Wiener and Brody state, caused by univalent Rh antibodies which because of their smallness pass into the foetal circulation during pregnancy and produce "coating" and rapid breakdown of the foetal red cells, thus causing a progressive anaemia and, in severe cases, stillbirth and hydrops foetalis. In this group the foetal antibody titre more closely approximates to that of the mother, and the severity of the disease corresponds to the height of the maternal titre. Kernicterus is not a common sequel, and, if they recover, the infants usually develop normally. Transfusion with Rh-negative blood of a suitable group is the best treatment.

In the third group—icterus praecox—maternal *alpha* or *beta* antibodies act as lethal agents on the red cells of infants with an incompatible blood group, a pathological extension of what has often been termed the "physiological" icterus of the newborn. Typical cases develop a greater or less degree of jaundice in a few days and clear up spontaneously.

In effect Wiener and Brody distinguish between bivalent and univalent antibodies produced as a result of sensitization of an Rh-negative mother by an Rh-positive foetus. They consider that the bivalent antibodies may as a result of thrombosis cause jaundice, erythroblastaemia without anaemia, and kernicterus, though in any one case all three conditions may not be present. The univalent antibody on the other hand causes haemolysis of the foetal red cells, jaundice, and anaemia, and in this group alone is transfusion of any value. From the practical standpoint they claim that by differentiating these two types of rhesus antibody in the mother the chances of kernicterus occurring in any given case can be foreseen even before birth.

This new theory receives striking confirmation from the work of V. C. Vaughan,[*] who studied erythroblastosis foetalis and the incidence of kernicterus in 72 infants. He confirmed the fact that cases of kernicterus tended not to develop gross anaemia and that indeed anaemia was sometimes conspicuous by its absence. While refusing to commit himself regarding the actual pathology and the serological mechanism of the condition, he agrees with Wiener and Brody that transfusion with Rh-negative blood is useless for this type of erythroblastosis, and is even inclined to advocate the trial of Rh-positive transfusion as a "sponge" for antibody transferred to the foetus during delivery.

Clearly no final conclusion has been reached, but these findings are important, and they serve as another example of the need for backing laboratory hypotheses by clinical observations.

PROTEIN DEPLETION AND RESISTANCE TO INFECTION

Does an inadequate diet adversely affect the capacity to respond to artificial immunization? This question is of topical importance, and in answer to it recent observations of Wissler[1] are of interest. He compared the response of groups of rabbits on a normal diet to two intravenous injections of a pneumococcal vaccine with that of groups kept for a long period on a diet containing one-seventh to one-fourteenth the amount of protein. Type I pneumococcus was chosen because rabbits are highly susceptible to this organism but can normally be readily immunized against it. The resistance of the animals to the intradermal injection of an infecting dose of pneumococci was tested six days after the last dose of vaccine.

The rabbits on the low-protein, low-calorie diet were lighter than the controls, lost hair and fat, and sometimes had ascites and hydrothorax; they were anaemic and had low serum-protein levels, due to deficiency of the albumin fraction; the total leucocyte count was unchanged, but there was some increase of granulocytes and decrease of lymphocytes. The average agglutinin response of groups of young and adult rabbits on the defective diet was much lower than in the normal group. In the former groups only 1 out of 13 adults and 2 out of 14 young animals survived the challenging dose, as compared with 6 out of 10 and 17 out of 19 in the corresponding control groups. The survival times of non-immunized rabbits of the various groups did not differ significantly. There was excellent correlation between a certain level of agglutinins and survival. The protein-depleted animals had only a small rise in the granulocyte count and a steep fall in serum-protein concentration during infection. In the rabbits with low resistance the skin lesion was spreading and oedematous, and, in contrast to the findings in adequately immunized animals, scanty interstitial agglutination and phagocytosis of the pneumococci were observed in it.

Similar results were obtained in a series of experiments with rats in which the infecting dose was adjusted according to body weight. When the quantity of food eaten was equalized in the low-protein and control groups the agglutinin response in the two did not differ, but the relative survival rates were similar to those obtained with rabbits. Unlike rabbits, rats possess some degree of natural resistance to pneumococcal infection, which was largely lost during protein-depletion. Mouse-protection studies failed to reveal any circulating antibody to explain this resistance, the loss of which could be counteracted by passive immunization sufficient to raise the agglutinin titre to the level usually obtained by active immunization of rats on the control diet. As with rabbits, the degree of natural and acquired resistance was related to the effectiveness of phagocytosis.

Under the conditions of these experiments it was much more difficult to produce resistance to infection by artificial immunization in animals kept on a grossly protein-deficient diet than in normal animals. This ineffective resistance was associated with a poorer humoral antibody response and probably with an impaired production of leucocytes following infection.

[1] *J. Infect. Dis.*, 1947, **80**, 250, 264.

NATIONAL HEALTH SERVICE ACT, 1946

POSITION OF CONSULTANTS AND SPECIALISTS*

OPINION BY COUNSEL

I have been asked to advise as to the position of consultants and specialists (hereafter called specialists) under the National Health Service Act, taking into account the questions submitted to the Minister by the B.M.A. and the replies of the Minister thereto.

The duty rests upon the Minister to provide the services of specialists at a hospital, health centre or clinic, or, if necessary on medical grounds, at the home of the patient. (Under Section 3.) The position of specialists under the Act is uncertain and in my view unsatisfactory, inasmuch as their rights and obligations are largely left to be determined by *Regulations to be made by the Minister.* (Sections 68 and 14.) No Regulations dealing with provision of specialist services under the Act have yet been made, and until such Regulations are made and published it is not possible to form any opinion whether specialists will be offered fair and equitable treatment under the Act.

I suggest that a request should be made to the Minister to consult the London Consultants Liaison Committee before he makes any Regulations as to specialist services under the Act.

1. Specialists Holding Appointments at Hospitals Immediately Before the Appointed Day

There is a marked distinction between the provisions of the Act as to general medical practitioners who wish to provide general medical services under the Act and specialists who hold an appointment at a hospital on the appointed day and who wish to provide specialist services under the Act.

Every medical practitioner who is engaged in medical practice (otherwise than as a paid assistant) is entitled under the Act, as of right, to have his name included in the list of medical practitioners undertaking to provide general medical services in his area if he makes an application at any time before the appointed day. (Section 34, Subsection 1.) *There is no provision in the Act giving a similar right to a specialist holding an appointment at a hospital on the appointed day.*

It is enacted by Section 68 that Regulations shall provide for the transfer and compensation of certain officers therein specified. Until, therefore, the Regulations are made, the position of specialists holding appointments at hospitals and particularly of honorary specialists is uncertain.

I interpret Section 68 (1) as meaning that, under the Regulations when made, all specialists (except possibly honorary officers) holding appointments, whether part-time or whole-time, at a transferred hospital immediately before the appointed day will be transferred in the case of a non-teaching hospital to the Regional Hospital Board, and in the case of a teaching hospital to the Board of Governors. I am not quite sure, however, whether the words "employed solely or mainly at or for the purposes of a hospital" are intended to cover a part-time appointment.

There is no provision in the Act which guarantees to specialists (whether whole-time or part-time) that, on transfer, they will be employed on terms and conditions and in circumstances not less advantageous than were applicable to their existing appointment at the date of the transfer.

There is no provision in the Act which would prevent the Regional Hospital Board or the Board of Governors from terminating the appointment of a specialist, after transfer, on short notice, or from compelling such specialist to relinquish his appointment by reason of his being required to perform duties which were not analogous with or which were an unreasonable addition to those which he was required to perform immediately before he was transferred.

There is no provision in the Act entitling the specialist (except some in whole-time employment) whose appointment is so terminated or relinquished to compensation for loss.

The answer of the Minister to Question 6 shows that he contemplates that on the appointed day the existing staffs of hospitals will be taken over by the Regional Hospital Boards or the Boards of Teaching Hospitals. It is not quite clear from the answer whether "staffs" includes part-time specialists or honorary specialists. It is clear, however, from the answer that the Regional Hospital Board and the Board of Governors of Teaching Hospitals will be expected by the Minister to review the services of their regions and to offer new appointments to their staffs either in their existing or in other hospitals.

On transfer, therefore, a specialist will merely hold a temporary appointment until he is offered a new appointment at the same or another hospital on such terms and conditions as the Board determine (subject to any Regulation made by the Minister).

In my opinion neither the provisions of the Act nor the answer of the Minister can be regarded as satisfactory or as affording such reasonable protection as specialists now holding appointments at hospitals can fairly claim.

I advise that every effort should be made to obtain in the Amending Act provisions similar to Sections 58, 59, and 60 of the Health Services Bill (Northern Ireland):

"Section 58. (1) All officers employed immediately before the appointed day solely or mainly at or for the purposes of any hospital transferred to the Authority under Section 23 of this Act shall on that day become by virtue of this section officers of the Authority.

"Provided that the foregoing provisions of this section shall not apply to:

(*a*) any person who has attained the age of 65 years on the day immediately preceding the appointed day;

(*b*) any person who elects in the prescribed manner that they shall not apply to him;

(*c*) honorary officers.

"(2) An officer of any hospital who, by virtue of the foregoing provisions of this section, becomes an officer of the Authority shall be employed by the Authority on terms and conditions (including conditions as to superannuation benefits) and in circumstances not less advantageous than were applicable to his employment with that hospital:

(*a*) on the twenty-first day of March, 1946, or

(*b*) where such officer was not employed by the hospital on that date, on the day on which he entered that employment.

"(3) Where, in any case to which paragraph (*a*) of the last preceding subsection applies, the terms and conditions applicable to the employment become, after the date specified in the said paragraph, more advantageous to the officer by reason of any increase of salary or other additional benefit, the Ministry may, if it thinks fit, direct that the right to that increase or benefit shall be included among the terms and conditions on which the officer is employed by the Authority; and where such a direction is given with respect to any officer the provisions of the last preceding subsection shall in relation to that officer have effect subject to the said direction."

"Section 60, Subsection (2). Subject to the provisions of this section, every officer employed by the Authority or the Board:

(*a*) who became such an officer by virtue of the provisions of Section 58 of this Act; and

(*b*) who within five years of becoming such an officer:

(i) relinquishes office by reason of his having been required to perform duties which are not analogous with or which are an unreasonable addition to those which he was required to perform immediately before he became such an officer;

(ii) from any cause other than misconduct or incapacity or his having attained the age of 65 years is removed from or required to relinquish office;

shall be deemed, unless the contrary is shown, to have suffered a direct pecuniary loss in consequence of this Act, and shall be entitled to compensation under this Act for that loss. Compensation under this subsection shall be payable by the body by whom the officer was employed as part of the expenses of the Authority or the Board as the case may be."

I also advise a definition of the words "officers employed." (*Section 68 of the Act.*)

*Issued by the subcommittee of the London Consultants Liaison Committee: Lord Horder (Chairman); Sir Reginald Watson-Jones; Dr. Geoffrey Bourne; Mr. A. Lawrence Abel; Mr. Eric Steeler (Secretary).

SPECIALISTS HOLDING "HONORARY" APPOINTMENTS IMMEDIATELY BEFORE THE APPOINTED DAY

As I have pointed out, the Regulations as to transfer which will be made by the Minister under Section 68 may contain exceptions and conditions in the case of honorary officers.

I gather, however, from the Minister's answer to Question 6 (though it is not quite clear) that specialists holding honorary appointments will be transferred to and become officers of the Regional Hospital Board if they consent to such transfer.

It appears from such an answer that they will then be offered a new appointment at their existing or other hospitals which (the new appointment) they will be free to accept or refuse. I apprehend that the terms and conditions of service will be similar to those applicable to a paid appointment except as to the emoluments.

It might, for example, happen that a specialist holding an appointment at Bristol be offered an appointment at Truro because of redundancy at Bristol. If, however, the new appointment were refused, it appears that the specialist would not be allowed to retain his existing appointment, and he might not be offered any alternative appointment.

In my opinion the safeguards which I have suggested with regard to whole- or part-time paid specialists should also apply to existing honorary specialists.

Another question which requires consideration is the possibility that in the course of time Regional Hospital Boards or Boards of Governors might tend to appoint more whole-time specialists and fewer part-time specialists until the majority or possibly the whole of such appointments were whole-time.

I cannot find anything in the Act which would preclude the Boards from adopting this course if they were or became minded to do so.

On the other hand, the Minister in several of his answers states that he anticipates that consultant and specialist appointments at hospitals should in most cases be part-time. He also states that if any Regulations are made under Section 66 he will exclude from them any provision of universal whole-time specialist services.

I advise that the specialists should ensure that the Amending Act implements the Minister's promise that hospital appointments for specialist staff will usually be part-time, so that the specialist service cannot become a whole-time service by Regulation.

COMPENSATION

The only persons who are entitled under the Act to be paid compensation are the persons specified in Section 68 (*e*) and 68 (1) (*f*). One of the essential qualifications is whole-time employment.

The right to compensation, however, is not conferred by an express clause in the Act itself, but will be governed by Regulations which are to be made by the Minister and which may contain exceptions or conditions. (Section 68.)

Moreover, the Act is silent as to the method of making a claim, the person or body by whom the claim is to be determined, the procedure for determining a claim, and to the right of appeal on fact or on law. Presumably the Minister proposes to provide for all these matters by Regulation.

I advise that the right to compensation should be conferred expressly by a separate clause in the Amending Act, and that this clause should contain provisions as to the determination of such claims by a Claims Tribunal and regulating the procedure upon the lines of Section 60 and the Sixth Schedule to the Irish Bill.

Inasmuch as the ordinary part-time specialist, honorary or paid, is not entitled to compensation, it is essential that he should be assured of security of tenure of his office with its existing facilities.

2. Appointment of Specialists to Hospitals

In the event of a vacancy for a specialist at a hospital after the appointed day, the appointment will be made by the Regional Hospital Board in the case of a non-teaching hospital, and by the Board of Governors in the case of a teaching hospital from persons selected by an Advisory Appointments Committee. (Section 14.)

The Minister, however, has power to determine by Regulation what classes of medical officers shall be appointed. (Section 14.)

The Advisory Appointments Committee will be established under Regulations and will consist (1) in the case of a non-teaching hospital of persons nominated by the Regional Hospital Board and the Hospital Management Committee of the hospital affected, and (2) in the case of a teaching hospital of persons nominated by the Board of Governors and the University with which the hospital is associated.

The representatives of the medical profession will be in a minority upon the Regional Hospital Board and the Hospital Management Committee.

There is therefore no guarantee that, on the occasion of a vacancy at a hospital, any specialists of the class of specialists concerned will be members of the Advisory Appointments Committee. Also there is nothing in the Act that obliges the Appointments Committee to consult the existing staff before making any selection for a new appointment.

I advise that the Act should be amended so as to provide: (a) that in the case of an appointment involving specialist services the Advisory Appointments Committee should include a specialist or specialists nominated by any organization which appears to the Regional Hospital Board or Board of Governors to be representative of the class of specialists concerned; (b) that before making their selection the Advisory Appointments Committee should consider any recommendations made by the specialists then holding appointments at the hospital affected.

3. Legal Rights of a Specialist on Appointment to a Hospital

On appointment to a hospital the specialist becomes an officer of the Regional Hospital Board or of a Board of Governors. His remuneration and conditions of service will be fixed by the appropriate Board, subject to Regulations made by the Minister. Presumably the specialist will be required to enter into a contract with the Board laid down by the Minister. The specialist's rights will depend on and be defined by that contract.

I advise that the Minister should be asked to state the terms of the contract, and in particular its duration, the rights of the Board to terminate it, and the grounds upon which the same may be terminated.

I advise that following the present practice the engagement should be until the attainment of an agreed age, terminated only for misconduct or incapacity.

I advise that the Minister should be asked to provide in an Amending Act that the specialist should have the right to appeal to a Tribunal comparable to that under Section 42, with an ultimate right of appeal to the High Court.

I have considered the latter half of the Minister's reply to Question 6, but in my view it does not provide adequate protection. Of course, if there is a breach of contract the specialist would have his remedy at law. If, however, the contract provides that it may be terminated by the Board by notice of a specified length, the Board could lawfully terminate the contract at the expiration of such notice without assigning any reason. Neither the Medical Committee nor a Whitley organization could, in my view, provide an adequate remedy against a capricious determination of the contract by the Board.

SPECIALISTS PROVIDING SPECIALIST SERVICES AT A LOCAL HEALTH CENTRE, CLINIC, OR AT THE HOME OF A PATIENT (SECTION 21, SUBSECTION 2)

It is not clear whether the "staff" whom a local health authority are required to provide at a Health Centre for specialist services will be employed by the local health authority or by the Regional Hospital Board or Board of Governors. Moreover the Act does not clearly indicate the person or body by whom a specialist will be employed for the purpose of providing specialist services at a clinic or at the home of the patient. Possibly the intention of the Minister is that all such specialists shall be employed by the Board of a hospital, but it is desirable that the position should be made clear.

4. Preservation of Existing Pay-beds in Hospitals

There is no obligation under the Act upon the Minister to preserve existing pay-beds in hospitals. Under Section 5 he *may* do so if, having regard to his duty to provide hospital and specialist services, he is satisfied it is reasonable. The Minister *may* allow any medical practitioner whether honorary or paid on the staff of a hospital providing hospital and specialist services to treat his private patients at that hospital or at any such other hospital and *may* make available such special accommodation. In this event the patient pays the cost of the special accommodation and the fees to the specialist not exceeding the maximum fee prescribed by Regulations.

In his answer to Question 2 the Minister says that private pay-bed accommodation is promised under the scheme and expressly provided for in the Act, and that it is to be assumed that at the outset of the scheme it will lie where it is at present, but the Minister cannot tie himself to an exact future distribution now. The Minister adds that the continuance of part-time specialists at hospitals accords with the intention of the scheme and there will therefore be facilities for them.

The existence of private pay-beds at hospitals is of fundamental importance to specialists, and I advise that a clause should be inserted in the Amending Act similar to Section 29 (2) (*f*) and 29 (2) (*g*) of the Irish Bill ensuring the preservation of such accommodation where it exists.

It is possible that after the appointed day the hospital accommodation will be found to be inadequate to meet the demand for non-paying beds and it is in my view likely that, notwithstanding the intentions of the Minister and of the scheme, the existing pay-beds may be utilized to meet the demand for non-paying beds. The Minister could shelter himself under the opening words of Section 5 if he found himself constrained to take this course.

I advise that the Amending Act should include a provision on the lines of Section 21 (4) of the Irish Act so as to make it clear that a hospital is entitled to establish new *pay-beds.*

5. Retention and/or Establishment of Medical Committees in Transferred Hospitals

Though there is power under Section 12 to appoint Medical Committees in hospitals subject to Regulations and directions given by the Minister, there is no express provision in the Act for the appointment of such Committees. It is clear, however, from the Minister's answer to Question 4 that he entirely agrees with the system of Medical Committees in hospitals and has expressed his view to Regional Hospital Boards and Hospital Management Committees and asked that every encouragement and facility should be given to this system.

Under the Act the medical staff of a teaching hospital has the right to nominate not more than one-fifth of the Board of Governors. No similar right is accorded to the staffs in the case of a non-teaching hospital or group of hospitals to nominate members to the Hospital Management Committee.

The Act merely provides that the Regional Hospital Board shall consult the medical staff and appoint some members of the Hospital Management Committee without being bound to accept their nominees. This might result in there being no representatives of the medical staff on the Hospital Management Committee.

I advise that the medical staffs of non-teaching hospitals should be accorded the same rights of nomination as have the medical staffs of teaching hospitals.

6. Acquisition of Land (Section 58)

The power of the Minister and of a local authority to acquire land compulsorily includes the power to acquire a hospital or clinic or nursing-home carried on for profit.

I advise that Section 58, Subsections (1) and (2), should be amended so as to exclude a "hospital" carried on for profit as is contained in the Irish Bill. (Section 67 (1).)

7. Freedom of Speech and Publication

By his answer to Question 5 the Minister states that the assurances already given cover complete freedom to publish views on the organization and administration of the Service as well as on clinical matters without obtaining any prior consent to do so. I understand that the Minister has declared his intention to incorporate a clause to this effect into the contracts of medical practitioners who undertake to provide any services under the Act. This is an important matter upon which the profession as a whole should come to a decision.

If the assurance of the Minister is implemented by a suitable provision in the contract of each medical practitioner (whether providing specialist or general medical services) he will for all practical purposes be as well protected as if there was a clause in the Act.

The prejudice which a medical practitioner would be most likely to suffer as a result of his public criticism of the Service would be that his contract might be terminated by the body which employs him. If the contract contains an appropriate clause (as promised by the Minister) public criticism of the Service could not be construed as misconduct which would entitle the employing body to dismiss summarily the medical practitioner. It is possible that the employing body might as a result of such criticism seek to terminate the contract of a medical practitioner without disclosing the real grounds for terminating the contract. This, however, might happen whether there is a clause in the Act or not.

I have already made some suggestions for the protection of specialists against a capricious determination of their contracts. The profession must decide whether they are prepared to rely upon the repeated assurances of the Minister on this question, knowing that there is no provision to this effect in the Act or in the Regulations published up to date.

Regulations (Section 75)

One of the most unsatisfactory features of the Act is that many of the important matters arising under it are not enacted in the body of the Act, but are left to be governed by Regulations. The Minister has very wide powers to make Regulations, and is not under any statutory obligation to consult the medical profession before he makes such Regulations.

I have already pointed out that the rights and obligations of specialists will be almost exclusively determined by or in accordance with Regulations.

I have considered the Minister's answer to Question 7. It is quite true that Regulations have certain advantages where flexibility is required. On the other hand they might equally be used to reduce as well as to increase the capitation fee of general medical practitioners or the emoluments of specialists, or to impose upon them more onerous duties or unfavourable conditions of service. Moreover, as Regulations may be modified or repealed by the Minister, where the existing rights of individuals are affected by the Act, they enjoy greater protection if the Act contains specific clauses defining those rights. I have already indicated some instances.

As to the Minister's power to make Regulations, I think that possibly the College of Physicians had in mind Section 1 of the Rules Publication Act, 1893. The application of this section to Regulations made under this Act is expressly excluded. (Section 73 (5).)

Under Section 1 of the Rules Publication Act, 1893, a Minister is required (*inter alia*) to give forty days' notice in the *London Gazette* of his intention to make Regulations. Any public body may inspect the draft Regulations and the Minister is required to consider the written representation of any public body interested before he makes the Regulations.

I advise that the Minister should be approached with a view to securing an amendment which provides that Section 1 of the Rules Publication Act, 1893 (or a suitable modification thereof), should apply to Regulations made by the Minister in future.

The Royal Colleges and the B.M.A. should be included in the definition of "public body" so as to enable them to inspect the draft Rules and to have the right of making representations.

Under the present procedure in Parliament, Regulations are seldom debated or submitted to detailed examination by the House unless the Special Committee recommends that the special attention of Members should be drawn to them.

Under this Act the power of the Minister is so wide and the area over which the power extends is so large that it is difficult to imagine any Regulation which could go beyond the scope of the Act.

SPECIALISTS AND THE NEW SERVICE

LONDON MEETING

A meeting of consultants and specialists of London and the Home Counties, summoned by the Marylebone Division of the British Medical Association, was held in the Great Hall, Tavistock Square, on April 22. The purpose was to consider the present position in view of the recent conversations with the Minister. There was an attendance of over 200. Mr. A. M. A. Moore presided.

The Recent Conversations

Lord Horder, who was one of the deputation to Mr. Bevan on April 12, said that it was a very friendly interview up to a certain point. The Minister was extremely conciliatory, obviously anxious that doctors should enter the Service, but his answers to a number of the questions (which Lord Horder thought not too well chosen) were evasive, and at the end it did not appear that the main position had changed materially. Certain small points were conceded, but always when it came to fundamentals—that is to say, the terrifically powerful position the Minister maintained in respect of a comprehensive service—the answer was in the negative. He himself would have liked more attention paid to the last question of all put to the Minister—namely, whether he agreed that the appointment of members of the profession to administrative and other bodies should be in consultation *and agreement* with representative bodies of the profession. The answer was that the Minister was ready to consult, but constitutionally the decision was his. At the conclusion of the questions the Minister asked Dr. Dain whether he would now be prepared to advise the profession to enter the Service. Dr. Dain wisely declined the invitation to give an immediate answer, and said that this was a sum in arithmetic and that he must take time to add it all up. The dictator then made himself obvious, and suggested that the blame for delay must be laid at the door of the B.M.A. and not at his own.

Since then there had been an "extraordinary hustle" over the second plebiscite. It was rather beating the air to discuss anything that evening except the position of specialists (a generic word for both specialists and consultants). General practitioners would make up their own minds in the plebiscite now being taken, but there remained a definite interest for the specialist apart altogether from the general practitioner. In his own view the general practitioner's freedom had not been safeguarded; he was being outwitted by political manœuvring. But as for the specialist, his position was as yet wholly undefined. The Act gave the Minister power to set up a specialist service in or out of hospital, but the terms of contract were not known. Therefore, although they would vote in the plebiscite—he would vote in the same way as he had done before, the position being in his judgment not virtually changed—he thought they had also to look at their own house and see if it was in order.

It was highly desirable (Lord Horder continued) that as soon as possible specialists should have a policy either to do something or to refrain from doing something until their knowledge of where they stood was more complete. He suggested that they should say to the Minister, "You have so far laid down no conditions of service in or out of hospital." He himself would stand very strongly for the availability of the specialist for domiciliary purposes if the doctor in charge of the case wanted help. But in or out of hospital the position was still entirely indefinite.

Lord Horder went on to refer to the setting up of the London Consultants Liaison Committee, whose first task it had been to discover where, legally, specialists stood under the Act. The opinion of Mr. Cecil Havers, K.C., had been sought, and copies of this opinion, fresh from the printer, had been distributed among those attending the meeting. Lord Horder urged that no contract be signed and no payment accepted until there was an agreed policy between a representative body of specialists and the Minister. (Applause.)

Mr. Naunton Morgan said that the overwhelming vote against working the Act as shown in the last plebiscite was not a vote on detail—the details of the Act were too complicated and abstruse for most of them to follow—but it was a vote of conscience against what had been done. He drew attention to one statement by Mr. Cecil Havers in the opinion just mentioned:

> The position of specialists under the Act is uncertain and, in my view, unsatisfactory, inasmuch as their rights and obligations are largely left to be determined by Regulations to be made by the Minister.

Until Regulations dealing with the provision of specialist services were made and published it was not possible to form any opinion whether specialists would be offered fair and equitable treatment under the Act.

Dr. E. C. Warner regretted that they had conceded the position with regard to the administration of voluntary hospitals. A scheme might have been worked out on a very different basis. Why should not the large hospitals have been placed in a similar position with regard to grants to that which obtained in the medical schools? They might have been given a State grant and allowed to administer it in their own way without hordes of officials being appointed to see how it was spent. The scheme of the University Grants Committee might have been applied in a larger sense. The Service came into operation in ten weeks' time, and yet specialists had not been given one word of help as to the nature of the scheme under which they had to work. Many things had to be clarified. Was it going to be possible for a consultant outside the Service to use hospital beds at all even in the private wards? Another point was that, on transfer, as Mr. Havers said, a specialist would merely hold a temporary appointment until he was offered a new one at the same or another hospital on such terms and conditions as the Regional Hospital Board determined. The Minister seemed to have adopted a more conciliatory attitude towards general practitioners than towards specialists. The speaker was anxious that they should not sell their birthright and the interests of their patients for a scheme over which they had no control whatever. Until they knew what the conditions of service were going to be, he did not feel that he could vote in the present plebiscite differently from the way in which he voted in the last.

Legal Opinion

Mr. Lawrence Abel reminded the meeting that, very largely due to the efforts of their chairman, Mr. A. M. A. Moore, a democratic scheme for the representation of all consultants and specialists had been brought forward and approved by the Council of the British Medical Association. He then gave a review of Mr. Cecil Havers's opinion which the London Liaison Committee had obtained. One point made by Mr. Havers was that every effort should be made to obtain in the Amending Act provisions similar to certain sections of the Northern Ireland Act, whereby every consultant, like every general practitioner, had the right to enter the Service if he wished. Mr. Havers also advised that specialists should ensure that the Amending Act implemented the Minister's promise that hospital appointments for specialist staff would usually be part-time, so that the specialist service could not become a whole-time service by regulation. Again, inasmuch as the ordinary part-time consultant (honorary or paid) was not entitled to compensation, Mr. Havers advised that it was essential he should be assured of security of tenure of his office with existing facilities. As to the legal rights of a specialist on appointment to a hospital, Mr. Havers advised that the Minister be asked to state the terms of the contract, and in particular its duration, the rights of the Board to terminate it, and the grounds upon which it might be terminated; that, following the present practice, the engagement should be until the attainment of an agreed age, terminable only for misconduct or incapacity, and that the Minister should be asked to provide in the Amending Act that the specialist should have the right to a tribunal comparable to that under Section 42 of the Act, with an ultimate right of appeal to the High Court. A clause should be inserted, as in the Irish Act, ensuring the preservation of private pay-bed accommodation where it existed, and a provision to make it clear that a hospital was entitled to establish new pay-beds. Mr. Havers was also of opinion that the medical staffs of non-teaching hospitals should be accorded the same rights of nomination to the Board of Governors as the staffs of teaching

hospitals possessed. There were several other points in this very useful opinion, many thousands of copies of which were being distributed.

A Change of View

Sir Reginald Watson-Jones said that since they last met in that hall an event had happened upon which it was difficult to speak but impossible to be silent. His meditations had led him to a certain conclusion. For two years he had persisted relentlessly and without faltering in his opposition to the National Health Service Act, which, he had believed, threatened the freedom of medicine. At a dinner over which he presided, when Mr. Attlee and Mr. Bevan were guests, he had declared: "I will not be a Civil Servant." During those two years he had spoken at meetings of the Council of the Royal College of Surgeons, sometimes in a majority, sometimes in a minority, once at least in a minority of one. Finally he had been and still was a trustee of the Independence Fund. With that background, if the conclusion at which he had arrived was that they should now accept service under the new Act, he trusted it would be accepted that he was no quisling, or one afraid of being in a minority, or one who, before he spoke, considered his personal advantage.

What was it for which they had been fighting, and how far had they succeeded? They had been fighting for the freedom of medicine, professional freedom, freedom from bureaucratic control, freedom to speak and publish and criticize, freedom for the pioneer, freedom for private practice alongside nationalized service. How far in the promise of an Amending Act had they succeeded? They had succeeded in that there would now be medical committees for every hospital; the medical committees of teaching hospitals would nominate their own representatives on governing boards, and although it was different with the non-teaching hospitals he believed that their representatives would be appointed too. They had succeeded in the matter of freedom of speech and publication, relating to administrative as well as clinical matters. They had the promise of an Amending Act to ensure that a whole-time State salaried service would not be brought in by Regulation. Their freedom was no longer threatened.

On what points had they failed? They had failed in securing the exclusion of the power of compulsory purchase of hospitals and nursing-homes carried on for profit. He would have liked to see a provision such as had been introduced in the Irish Bill making such acquisition impossible, but he could not agree with those who said that this compulsory acquirement would be a way of destroying private practice. Such destruction would not come about by acquiring the building but by acquiring the surgeon. They had failed in another matter. Staff appointments would be made not by medical but by appointments committees; but was that an important principle, or was it one on which they might have two views? They had failed to secure a firm promise of security of tenure of a surgeon in his present post. But he wondered whether that was an object which they could expect to achieve.

He submitted that the points on which they had succeeded were points of principle, and the points on which they had failed were points of detail. Two months ago when the consultants and specialists held a meeting in that hall they were considering fundamentals. Fundamental principles had been challenged, and the plebiscite, with its 94% "No" vote, was the answer. They were now considering debatable details.

"We have won a most resounding victory. From the lack of enthusiasm here to-night I begin to wonder whether that is true. But the most important point is that we have demonstrated that the profession when united can alter the decision of a Minister and a Government. I agree with what Mr. David Eccles, M.P., says in *The Times* this morning: 'The doctors have learned the secret of this power [the power of a united profession] and if they use it wisely and do not throw it away by splitting on unpopular issues they can stand up to this Minister and any of his successors.'

"Our duty now is twofold—first, to say that we acknowledge the concessions which have been made and accept the assurances, and secondly, and no less important, to watch every Regulation that is issued and to see in fact that these promises are implemented."

The speaker quoted a passage from Edmund Burke, and added: "We have achieved a victory which has determined our liberty; let us now achieve the order without which that victory means nothing."

Stipulations before Agreement

Dr. Geoffrey Evans said that it was a pyrrhic victory which had been won. He recalled that in 1929, when he was honorary secretary of the London Voluntary Hospitals Committee, pains were taken to secure for voluntary hospitals an equal status with municipal hospitals, and after conversations with Mr. Neville Chamberlain, then Minister of Health, a clause was inserted in the Local Government Act, 1929, that if there were extensions of beds in municipal hospitals they should be made in consultation with voluntary hospitals and vice versa, so that the hospital service of London might go forward in a co-ordinated manner. But when the Act was passed it was found that the clauses inserted had a legal interpretation which was not what the Minister nor they themselves had intended. They must suppose that the Minister of Health had good intentions, but he thought it ominous that eleven weeks before the Service was due to begin specialists were in ignorance as to their position. He felt that they should withhold service until what they required was in writing, and that in writing they should secure the position set out by Mr. Havers with regard to specialists holding honorary appointments immediately before the appointed day, the preservation of existing pay-beds in hospitals, the rights of nomination by medical staffs of non-teaching as of teaching hospitals, and freedom of speech and publication.

Mr. Dickson Wright said he was unable to see that the Minister had offered them anything of real value in these new conversations. It was not possible for the Minister to give the assurances asked of him. There were already a large number of whole-time people in the Service, and there was nothing to prevent a Minister increasing the whole-timers to the detriment of the part-timers, until perhaps he had ninety-nine of the former to one of the other, when he could still say that he had not gone back on his word. The voluntary hospitals could well have carried on. It was not fair to say that they had failed. The truth was that the Government had ruined them by Regulations and finance and undermined their subscription income. He did not think medical committees of the slightest value if they did not elect members of the staff; they merely became grousing bodies.

Dr. Geoffrey Bourne said he respected everything about Sir Reginald Watson-Jones except his credulity. No politician could go further than the first few steps of his career unless he learned how to change with the wind. Supposing the Service came into operation, people would soon be asking: "Where are the specialists whom we are told we could call in? Where are the health centres?" There would not be enough specialists to go round, and by Regulation the Minister would say to many of the part-time people: "Your contracts will be terminated in a month's time," and at the end of that month these "displaced persons" would be offered new whole-time jobs in other hospitals. The "spreading" was socialist policy, but a time would come when the spreading would prove too thin.

Mr. N. Ross Smith declared that their own safeguard was to have the principles they had fought for incorporated in the Act itself. He believed Lord Horder was right in suggesting that this move of the Minister was nothing more than a piece of political tactics. Sir Stanford Cade, while complimenting Sir Reginald Watson-Jones on his courage, said that in his belief this great "victory" was wholly a mockery. None of them were fighting for the potential pay that the Spens Committee might vote, but for their professional freedom, which he did not believe could be preserved under the existing Act without amendments to meet all the points brought forward by Lord Horder and others. If it was possible for the House of Commons in 24 hours to postpone the death penalty for five years, surely this Service could be postponed for a little beyond July 5.

Dr. G. J. Sophian said that what Mr. Bevan wanted was that they should surrender their arms whereby they defended themselves against his machinations. Mr. Jennings Marshall supported the view that they should decline to have anything to do with this Act until their own position was clearly stated. Mr. Lyle Cameron said that the previous day he had met someone just returned from Italy who had told him that the

resistance which the British doctors were putting up against regimentation was a point made by the winning side in the Italian elections.

Sir Reginald Watson-Jones, in reply to a question whether he would abide by the decision of the majority of the profession, said that he had been and still was a trustee of the Independence Fund, and if the majority of the profession did not enter the Service of course he would abide by that majority. (Applause.) His earlier observations were not the result of "credulity" but were based on an estimate of how best to make tactical use of their strength.

Lord Horder moved the following resolution:

That this meeting advises specialists not to enter into any contract under the National Health Service Acts until conditions of service have been agreed with the Minister.

This was carried by 196 votes to 1; there were 9 abstentions.

ACCIDENTAL SYPHILIS

BY

R. R. WILLCOX, M.B., B.S.

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"The first step, in order that we should understand syphilis, is to recognize that it is by no means necessarily a venereal disease."—*Sir Jonathan Hutchinson.*

Syphilitic chancres are genital in 95% of cases, and the majority of the other 5% arise in or around the mouth, many of these lesions being acquired through predominantly sexual acts. Not more than 50 examples of non-sexual accidental infection were found in over 35,000 syphilitic patients examined (Moore, 1944). The effect of such modern statistics and of the observed behaviour of the organism outside the body is that towels, bedding, cooking utensils, drinking-vessels, pipes, and the like are now far less often blamed for spreading the disease: in this connexion glass-blowing was once considered a dangerous occupation. It is realized that for the spirochaete to remain viable for transmission the presence of moisture is necessary. In 1878 Lane wrote: "I believe, also, the use of public water-closets at railway stations, hotels, and clubs may be a not very infrequent cause." Since that time this convenient conception of the lavatory seat has fallen into almost complete disrepute, and any such excuse offered by the patient is, perhaps not openly, derided by the clinician; yet there would seem to be no reason why transfer of moist matter should not occasionally occur by this means. It is, however, universally agreed that sexual intercourse is by far the most frequent cause and that kissing, albeit innocent, takes second place.

An example of infection by kissing was seen in the Army. A youth contracted a lip chancre on Christmas Day, when he was on sentry duty at the periphery of a remote camp in Scotland, and subsequently passed the disease in a similar manner to his fiancée. Schamberg reported oral transmission to seven young girls from one man in a kissing game (Stokes *et al.*, 1944), and there is no doubt that the larger the number of secondary syphilitics the greater the danger of such infections, but with modern methods of diagnosis and treatment this danger is becoming minimized.

Chancres have been reported on almost every part of the body; digital chancres in dental surgeons, gynaecologists, midwives, and oto-rhino-laryngologists, and conjunctival varieties, are examples. Lane mentioned the case of an unhappy surgeon who had the misfortune to contract a digital chancre from an obstetrical case and was later forced to pay heavy damages for passing on the disease during another confinement. Recently I saw a primary lesion in the left axilla, and though no explanation could be found as to its presence the patient showed no surprise.

Extragenital infection was once much more common, and if the thesis that syphilis and yaws are caused by the same organism, and that the former has developed from the latter, is correct, then it must be admitted that syphilis was originally entirely extragenital, being spread by contact and possibly even by flies. Intermediate forms, in which infection still occurs predominantly by this means, exist to-day as bejel, pinta, and "irkintja"—Australian boomerang leg (Hudson, 1946).

Such intermediate forms have been reported as outbreaks in North-Western Europe. In 1694 a disease called "sibbens" raged in the West of Scotland, and blame for this was placed on Cromwell's army. It was spread not only by coition but also by contact—kissing and suckling, and through drinking-vessels and utensils. Oral lesions were as prominent as genital manifestations, but it must be borne in mind that a woman with a primary sore on the cervix might show the first obvious symptoms in the mouth. Children were also affected, many possibly by suckling. "Radesyge," "the foul disease" of Norway and Scandinavia of the eighteenth century, the spread of which was aided by the fuel-saving custom of "bundling," was believed to have been of a similar nature, as were "Amboyna pimple" of the Moluccas and "Schlerlievo" of the Adriatic coast during the nineteenth century.

In those times mercury was the only effective means of treatment, and this was often delayed until the appearance of secondary signs, so that a diagnosis of "confirmed lues" could be made. This delay, the less-advanced views concerning the advisability of bathing, and the practice of allowing wet-nurses to assist in the suckling of children were the predisposing causes of spread of the infection. In 1752, at Nerac in France, some 40 women and children, in addition to numerous male consorts, were infected as a result of transmission by wet-nurses after one had contracted a nipple chancre from a congenital syphilitic infant.

Syphilis has been inoculated deliberately by the physician on numerous occasions. Hunter's unfortunate experiment in 1767 is perhaps the most famous; but that of Bell, who in 1792 published an account of his failure to transfer syphilis to three medical students smeared subpreputially with gonococcal pus and his subsequent success with two students when syphilitic matter was applied, deserves fuller mention. Wallace, in 1835, infected five healthy persons with matter from a secondary syphilitic, and thus proved that this stage of the disease was indeed infectious—a fact which Hunter and Ricord, as a result of more cautious lukewarm experiments confined to those already infected, had previously erroneously denied. Similar experiments also proved the infectivity of blood, and the prophylactic action of mercury was vividly demonstrated by the human experiments of Metchnikoff.

Apart from these calculated performances, the medical profession has been responsible for its fair share of the spread of extragenital infections. Cupping, as part of the ritual of celebration of St. Luke's Day, accounted for 180 cases at Brno, in Moravia, in 1578; though cynics will suggest some other feature of the celebrations as the most likely cause. In Hunter's time cases arose after transplanting teeth—a practice then in vogue. If the transfer was made too soon, or from a living person, a chancre occasionally developed after an appropriate interval in the socket of the recipient.

Vaccination was another great source of infection, and by employing the arm-to-arm technique the presence of an infectious syphilitic infant early in the chain might have serious results. Lancereaux (1868) referred to 351 persons known to have been inoculated with tainted serum; of these 258 contracted the disease. In 1870 Hutchinson published a series in which 10 out of 12 children were affected, and two years later a further series showing 15 possible infections out of 26. In one series of 46 most of the children, with their mothers—not to mention the fathers—became afflicted, and there were 19 deaths among the children. To-day this kind of tragedy is almost unknown, and the possibility is scarcely taught to the rising generation of medical students, though the textbooks used by our fathers contained tables of differential diagnoses concerning vaccinial syphilis. I have seen a primary yaw develop in a vaccination site, but it is to be hoped that the two infections were not acquired simultaneously.

Eustachian catheterization was another cause, and at a meeting in Paris in 1861 13 cases due to this procedure were reported. In more recent times blood transfusion has occasionally been a means of transmission, even during the incubation period of

the disease (Moore, 1944). Tattooing also has produced an occasional case. Hutchinson (1905) published a startling photograph of three chancres developing in the forearm over a tattoo mark of the Crucifixion. The Jewish rite of circumcision has also produced oral lesions in the rabbi, and the spitting of disinfectants has caused the reverse at a precocious age in the subject. Murrell and Gray (1947) described five cases of acquired syphilis in children at Edinburgh and those of two adults who contracted extragenital lesions as a result of fondling a congenital syphilitic infant. One child, prone to sucking things, was said to have found a condom in the park—a mode of infection also cited by Stokes.

The rather flimsy excuse for writing this article has been the recent experience of a lip chancre in a young woman obtained from her fiancé, who apparently had also obtained the infection by innocent means, though this is by no means completely proved.

The woman, a virgin aged 25, had had a chancre on the upper lip for nearly four months before she was referred for treatment, by which time she showed well-marked secondary signs of rash, adenitis, condylomata about the anus, and mucous patches on the vulva and lower lip. *Treponema pallidum* was recovered from the condylomata, and the serology was strongly positive. She denied any history of intercourse, though she had recently warmly welcomed her fiancé after his return from the Far East. He gave a history of intercourse in Java just over twelve months before, but two months later a serological test gave negative results. He was now well and no signs were detected. The serology, both Wassermann and Kahn, proved strongly positive, and detailed questioning revealed that ten months previously he had struck a man in the teeth with his fist and had broken the skin. This wound went septic, and though dressed at hospital with frequent antiseptics it refused to heal for six weeks, the turning-point being the application of penicillin cream in the fourth week. A well-marked cicatrix on the knuckle of the right hand was shown in evidence, and the epitrochlear gland on that side was just palpable. I had previously seen another patient from the same area who had been infected by a bite on his chest from a native.

These examples are cited to show: (1) that non-sexual transmission is no great rarity; (2) that there is no reason for not giving the benefit of the doubt to persons with a positive serology who deny all history of previous genital disease or of sexual intercourse; and (3) that the possibility of extragenital infection—yes, even the water-closet seat—should be accepted at least in women and not conceded as a favour with the tongue in the cheek.

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REPORT ON DISPENSING

In 1947 the Minister of Health and the Secretary of State for Scotland set up a Working Party "to investigate the differences in the work of pharmacists in England and Scotland in the dispensing and supplying of medicines and appliances, with particular reference to the position likely to arise under the National Health Service."* The Working Party also included Wales in its survey. Its composition was as follows: W. Penman, F.I.A. (Chairman); D. A. Bryan, M.P.S.; G. H. M. Graham, M.P.S.; A. A. Meldrum, M.P.S.; and J. Shields, M.P.S. Associated with it was a steering committee, of which Mr. Penman was the chairman, composed of officials of the Ministry of Health and of the Department of Health for Scotland, the Secretary of the National Pharmaceutical Union, and a representative of the Pharmaceutical Standing Committee (Scotland).

The Chairman decided how many and which pharmacies should be visited. The number selected was 300, of which 215 were in England, 25 in Wales, and 60 in Scotland. They were chosen, so far as possible, to provide a random sample from selected areas. Visits were also made to a few selected pharmacies giving a comprehensive service of the highest class, and to pricing bureaux. No inquiries were made into dispensing done under contract with doctors, dispensing done for institutions such as hospitals and infirmaries, and "counter prescribing." The four pharmacists in the Working Party were divided into two teams, each team containing one representative of England and Wales, and one of Scotland. A trial tour was made initially in Devon and Cornwall. A questionary was also sent to certain pharmacies not visited.

* The report will be published by H.M.S.O.

Formularies and Standardization

The Working Party points out that it is generally claimed that there is less use of formularies in Scotland than in England and Wales, and broadly speaking it substantiates this claim so far as mixtures are concerned. It found that of the National Health Insurance prescriptions for mixtures dispensed during July, 1947, 83.1% in England were based on national and *B.P.C.* formularies against only 3.5% in Scotland. In Scotland medical men are more inclined to use repeatedly what are virtually their own formulae, and there were 18.9% of such repeated prescriptions. Non-identical mixtures comprised 16.9% in England and 77.6% in Scotland. The corresponding figures for privately prescribed non-identical mixtures were 53.4% in England and 91.7% in Scotland. There was in fact a much less frequent use of formularies in the case of private prescribing, and a corresponding increase in non-identical formulae, than in the case of N.H.I. prescribing.

In the case of ointments, creams, and pastes those prescribed according to formulary were 93% in England, 95.8% in Wales, and 71.2% in Scotland; those according to non-identical formulae, 7% in England, 4.2% in Wales, and 17.9% in Scotland. In addition, 10.9% in Scotland were prescribed according to doctors' own formulae. The report points out that, as opposed to the practice in regard to mixtures, most formulary ointments are bought from wholesale houses in the form in which they are dispensed. There is no appreciable divergence of practice where tablets are concerned, for they also are bought wholesale. These three groups of medicaments comprise about 65% of the total prescriptions. Proprietary preparations account for another 5%, and the remaining 30% consists of miscellaneous articles such as glandular preparations, linctuses, appliances, and so on.

Ingredients and Prescriptions

It was found that in Scotland the number of doses per mixture is, on the average, higher than in England and the volume of the mixture smaller. In England ten- or eight-ounce bottles, containing tablespoon doses, are most commonly prescribed, whereas in Scotland the standard is a six-ounce bottle containing dessertspoon doses. There is no evidence that there are more ingredients in a Scottish than in an English prescription; indeed the figures indicate that on an average there are fewer ingredients in a Scottish prescription for both mixtures and ointments.

Stock mixtures are more popular in England than in Wales or Scotland, the average number kept in the English pharmacies visited being 13.6, in the Welsh 2.3, and in the Scottish 2.6. Two mixtures almost universally kept in stock were compound acid mixture of bismuth with pepsin, *B.P.C.*, and compound bismuth mixture with pepsin, *B.P.C.* Practically all stock mixtures used in England, apart from these two, are compounded on the premises by the pharmacist or his staff. Concentrated mixtures bought from wholesale houses are rarely used.

The Working Party, commenting on this difference of opinion about the desirability of using stock mixtures, points out that the Scottish attitude is that each prescription should be regarded as a thing apart, since it is prescribed for a particular patient. This involves more work and may lessen the monetary reward. The English pharmacist, on the other hand, would probably argue that there must be small errors in dispensing the individual prescription and that these are greatly reduced by dispensing from a stock mixture. He might add that he uses up the stock mixture in a day or two so that it does not become stale. He therefore saves his own and his customer's time.

Quality of Pharmacies

The Working Party classified the 300 small pharmacies into "poor," "satisfactory," and "good." Only one or two of the "poor" could be described as "bad." The "good" were establishments "not necessarily large, but of a definitely high class."

In England there were 2.3% poor, 90.7% satisfactory, 7% good; in Wales 8.3% poor, 83.4% satisfactory, 8.3% good; in Scotland 5% poor, 78.3% satisfactory, 16.7% good. The report shows that the standard is high and that the Working Party held the unanimous opinion that no exception could be taken to the system in either England and Wales or Scotland, and adds that it would be a mistake to compel either section of opinion to work on the lines of the other.

Doctors and Pharmacists

In England about 80% of the doctors do their own dispensing for private patients, whereas in Scotland only about 12% do so. The Working Party comments that under the National Health Service Scottish pharmacists will not have any appreciable increase in the total volume of dispensing because of reduction in private dispensing, while English pharmacists will have considerably more dispensing.

The Working Party next investigated the variation between the three countries in the respective proportions of N.H.I. and private dispensing by pharmacists. It found that in England and Wales combined N.H.I. dispensing amounted to about 77% and private to 23%; in Scotland the figures were 35% and 65%.

Information was obtained on the ability of pharmacies to cope with the increased business likely under the National Health Service. The Working Party concludes that (*a*) in about 80 to 90% of cases in England and 65 to 75% in Scotland it will be necessary to enlarge the *dispensaries*, but (*b*) only in about 10 to 15% of cases in England and under 5% in Scotland will it be necessary to enlarge the *premises*. The expense of preparing for the National Health Service will therefore fall more heavily on English than on Scottish pharmacists. Wales is in a worse position than both. The Working Party concludes that in most cases extra staff will be required for the extra dispensing, but they need not consist entirely of qualified or trained dispensers.

Remuneration

The Working Party considers that "certain differences of practice" between the countries are established and likely to continue under the National Health Service. It therefore considered whether these differences justified the continuance of differences in remuneration. It indicates, however, that in general no differences in remuneration exist at present, and it has therefore devised a uniform tariff embodying the following features:

(1) Where the work involved is the same, the fee should be the same. If the work is more onerous or more responsible than other work, the fee should be larger for that work, wherever it is performed.

(2) A suitable uniform definition of what is an ingredient.

(3) A built-up basic price for small quantities of drugs, the same as, or similar in effect to, the present Scottish device.

(4) When a built-up basic price is impossible or unsuitable, a uniform percentage on the wholesale price, but not necessarily the same percentage for every class of dispensing.

(5) Treatment of refund of purchase tax on a uniform basis.

(6) Suitable arrangements for payment for containers.

(7) A uniform but elastic scale of dispensing fees. The dispensing fee should consist of a comparatively small constant or universal fee, to which should be added a further sum depending upon the number of doses in some cases, or the number of ingredients, or on a combination of the number of ingredients and doses. In the case of ointments, a quantity factor would have to be introduced.

It concludes that a basic fee could be determined which could be applied to a very wide range of prescriptions, and that this could be adjusted for mixtures, ointments, tablets, appliances, etc. Certain pharmacies provide services such as bacteriological work, special analyses, and the supply of surgical and anaesthetic apparatus. The Working Party considers that under the National Health Service pharmacists should be allowed to continue to provide these services.

THE SEVENTH BRITISH PHARMACOPOEIA

MANY CHANGES

The General Medical Council is publishing the new *British Pharmacopoeia* with effect from Sept. 1, 1948, when this issue will supersede previous issues for all purposes. This volume of over 900 pages is the seventh of its series. The first "Book containing a list of medicines and compounds," to quote the Medical Act, appeared in 1864. A second was published in 1867, and an Addendum in 1874. The third appeared in 1885, and a further Addendum in 1890. The fourth was issued in 1898, and a Colonial and Indian Addendum in 1900. The fifth was brought out in 1914, and the longest interval—eighteen years—elapsed before the sixth was published in 1932. In 1933 the Pharmacopoeia Commission, which was charged with the preparation of the volume, was reconstituted; an Addendum was published in 1936, and the Commission proceeded to prepare a new *Pharmacopoeia* with a view to its publication in 1942, in accordance with the principle that ten years should be regarded as a reasonable interval between successive issues. It was also expected that the middle of each ten-year period would coincide with the revision of the *American Pharmacopoeia*. The war, however, delayed publication, but between 1940 and 1945 six further Addenda were brought out.

Pharmacopoeia Commission

The Pharmacopoeia Commission has had as its chairman Prof. J. A. Gunn, who succeeded the late Dr. A. P. Beddard in 1939. The other members were Mr. R. R. Bennett, Prof. H. Berry, Prof. O. L. V. S. de Wesselow, Prof. D. M. Dunlop, Sir Percival Hartley, Mr. B. F. Howard, Dr. D. Hunter, Prof. W. H. Linnell, and Mr. T. Tickle, with Dr. C. H. Hampshire as secretary. Prof. Gunn, Mr. Bennett, and Mr. Tickle were members of the Commission which prepared the 1932 volume. The Commission was assisted by 12 committees. The Clinical Committee had as its chairman Prof. de Wesselow, and among its members were Sir Ernest Rock Carling, Sir Francis Fraser, Sir A. M. H. Gray, Sir P. H. Manson-Bahr, Prof. J. A. Ryle, Sir C. P. Symonds, and Prof. L. J. Witts. Other committees were concerned with pharmacology, biological products, pharmacy and pharmacognosy, general and pharmaceutical chemistry, also with vitamins, ointment bases, nomenclature, and doses. Acknowledgment is made of valuable assistance and suggestions from medical and pharmaceutical authorities, including the Royal Colleges and Corporations, the Royal Society of Medicine, the British Medical Association, the Pharmaceutical Society, and other bodies in this country and in the Dominions and Colonies.

Newly Included Monographs

The number of monographs in the new *Pharmacopoeia*, each dealing with a separate preparation, is about 800, and there are 24 appendices describing the various tests, determinations, and assays. The number of articles and preparations which have been included in this *Pharmacopoeia* and do not appear in that of 1932 as amended by the Addenda and notices in the Official Gazette is 155. Among these are 57 injections, 18 tablets, 10 vaccines, and 9 sex hormones. The new injections include those of adrenaline, antimony and potassium tartrate, antimony and sodium tartrate, apomorphine hydrochloride, bismuth and sodium tartrate, caffeine and sodium benzoate, dextrose, digoxin, emetine hydrochloride, heparin, morphine and atropine, neoarsphenamine, hydnocarpus oil, progesterone, sodium bicarbonate, sodium sulphadiazine, sulpharsphenamine, sodium sulphathiazole, and tryparsamide, among others.

Compressed tablets have been dealt with on the same lines as in the Addendum published in 1945. The new tablets include those of acetylsalicylic acid with phenacetin, digitalis, digoxin, ergot, methyltestosterone, methylthiouracil, and thiouracil. The vaccines added include those for acne, cholera, dysentery (Flexner), whooping-cough, and plague, a staphylococcal vaccine, and "vaccinum tuberculinum."

The number of substances in the hormone series has been increased, especially by the addition of six members of the group generally designated sex hormones. In this group several substances prepared synthetically and having physio-

logical actions similar to those of natural hormones are included. While the purity of most of these can be determined by chemical and physical tests, biological methods are necessary for the assay of others and appropriate methods are described.

Other newly introduced monographs are concerned with benzyl alcohol, brilliant green, calamine, colchicine, dicoumarol, emulsion of liquid paraffin, ergotamine tartrate, dry extract of hamamelidis, heparin, dry lemon peel, neostigmin bromide, picrotoxin, potassium chloride, saccharin, tri- and tetra-chlorethylene, thiouracil, and zinc peroxide. A few suppositories are new to the *B.P.*—namely, those of cocaine, of bismuth subgallate, of hamamelidis, and of the last-named with zinc oxide.

Since the prescribing of fresh infusions in medical practice has continued to decline, the principle of preparing infusions from concentrated preparations has received full recognition. The monographs in this section include those on infusions of orange peel, senna, clove, calumba, quassia, senega, and one or two others. The arrangement of formulae for ointments and creams has been extended by the inclusion of certain newer bases, the formulae being designed to provide bases of different types.

Penicillin and Its Preparations

The sections relating to penicillin and its preparations comply with the regulations made under the Therapeutic Substances Act, and are in accord with the state of knowledge at the time the *Pharmacopoeia* was completed. Although the existence of different penicillins was known, the International Conference on Penicillin, which was called in 1944 by the Permanent Commission on Biological Standards of the Health Organization of the League of Nations, recorded its opinion that as a temporary measure it was desirable and possible to adopt as an international standard a pure preparation of sodium salt of penicillin II (or G), and to define an international unit in terms thereof. Advances in knowledge continue to be made relating to the different kinds of penicillin, the conditions under which they are produced in culture, their biological properties, and the possibilities of their application in medicine. When reliable and practicable methods for the estimation of different penicillins are devised and reference standards for their assay are adopted by international agreement it may be expected that due recognition will be given to these advances.

Vitamins A, B, C, and D, with appropriate methods for assay, are included. Of the vitamin B complex the constituents aneurin hydrochloride, riboflavin, nicotinic acid, and nicotinamide are described. So far as possible these substances are controlled by chemical and physical tests, but biological assays are described where necessary.

Some new antitoxins and vaccines have been added, as has protamine zinc insulin. The methods of preparing tinctures follow the general principles of the last volume, but no new tinctures are introduced. The description of methods of preparing sterilized materials for parenteral injection has been revised and extended. The sterilization methods described are designed to cover the preparation of such materials on either a large or a small scale.

Deletions and Changes

As many as 145 monographs which appeared in the 1932 *B.P.*, or its Addenda, have been deleted from the new *Pharmacopoeia*. These include in the first place 17 tinctures, among them those of asafetida, concentrated capsicum, cinchona, krameria, concentrated quassia, and quillaiae. The four plasters given in the 1932 edition also disappear—namely, those of belladonna, cantharidin, colophony, and lead. Other deletions are ammonium carbonate (now represented by ammonium bicarbonate), acetone, dilute hydrocyanic acid, dehydrated alcohol, amylocaine hydrochloride, cinchona, copaiba, iron and quinine citrate, glycerin of alum, guaiacol, effervescent sodium sulphate, strophanthin, and trinitrophenol.

The deletions, as has been stated, include all the fresh infusions, also a number of injections—iron, mercury, and sodium morrhuate, among others—and certain of the solutions, such as strong solution of ammonia, solution of arsenious and mercuric iodides, solution of irradiated ergosterol, solution of glyceryl trinitrate, simple solution of iodide, and blistering liquid. Some oils disappear, including those of Siberian fur and of sandalwood; also pills of aloes and asafetida and of aloes and iron; certain of the syrups—ferrous iodide, ferrous phosphate with quinine and strychnine, and ferrous phosphate with strychnine—and tablets of hexamine and of sulphapyridine, with others. Three sera are deleted—the anti-dysenteric serum (Shiga) and the anti-pneumococcus I and II. Finally some crude drugs appear no more, such as buchu, copaiba, jalap, linseed, and lobelia.

A few changes in name are made. For example, scammony resin becomes resin of ipomoea, and g-strophanthin becomes oubain. In a few articles and preparations there are certain changes in composition, and in still fewer cases changes in strength. The most important of these last is in the solution of hydrogen peroxide, which is now to contain officially 5 to 7% w/v of H_2O_2, instead of between 2.5 and 3.5%, corresponding to about twenty times instead of about ten times its volume of available oxygen.

Tests and Descriptions

The requirements of this *Pharmacopoeia* have been made to correspond, wherever possible, with the provisions of the international agreement made in 1930 for the unification of the pharmacopoeial formulae for potent drugs. It has not, however, been considered advisable as a general principle to adopt the practice of weighing liquids as well as solids. With few exceptions, liquids are measured by volume and not by weight, a practice more convenient both to prescribers and to pharmacists.

The monographs are set out with great clarity and precision. The custom has been continued of giving at the head of each monograph the Latin title. The American example of using English titles has not been adopted. The title is followed by the customary abbreviation and by the English title, this last not necessarily a literal translation. One change may be noted. The statements under the heading of "Characters" in the case of substances of known and definite chemical composition were formerly intended to be "descriptive of such physical and sensory properties of the substance as might be of importance for the medical practitioner and dispenser." In future, however, these statements are to be considered as constituting an integral part of the official standard. One of the General Notices states:

> All statements contained in the monographs, with the exception of chemical formulae given at the beginning of the monographs, constitute standards for the official substances. A chemical substance, crude drug, or preparation is not of pharmacopoeial quality unless it complies with all the requirements stated.

The arrangement of the monographs has been improved; graphic chemical formulae are provided, and the tests are set out under appropriate side-headings. In the case of a chemical substance there is first given the permissible but not obligatory method of preparation, followed by the percentage purity, the description, solubility, identification, various physical standards where these apply, the limit tests, and finally the assay. In the monographs describing crude drugs the first paragraph states the biological source, and the description is given where necessary under the headings "macroscopical" and "microscopical."

The doses mentioned in the *Pharmacopoeia* are not authoritatively enjoined as binding upon prescribers. They are intended simply for general guidance, and represent, unless otherwise stated, the average range of quantities which are generally regarded as suitable for adults when administered by mouth. The doses are expressed both in the metric system and in the imperial system, and attention is drawn to the fact that the relation between the metric and the imperial doses of a given preparation as set forth in the test is of only approximate equivalence.

For all processes, chemical or pharmaceutical, the metric system of weights and measures is employed. One alteration is the replacement of the abbreviation "mil." as a short designation for millilitre by the term "ml." Weights are given in milligrammes, contracted throughout to "mg.," or in grammes, contracted to "g." in tests and formulae and to "G." in doses.

The work is being published for the General Medical Council by Constable and Co., Ltd., but the price has still to be announced.

Correspondence

Gesture of Peace

SIR,—Mr. Bevan has made a gesture of peace. How are we to respond? At first he spoke rather as a dictator, somewhat offensively and insolently, and rightly we objected, claiming that in the interests of the public we must retain our freedom. Now Mr. Bevan has conceded the major point at issue. He has sacrificed in the national interest the point his party had repeatedly stated to be part of its programme. On our side should we not meet him by conceding minor points of difference that remain and trusting the Parliaments and Governments we elect to deal fairly and reasonably?—I am, etc.,

Banstead, Surrey. HERBERT CAIGER.

Minimum Requirements

SIR,—We may all welcome the improved atmosphere consequent upon Mr. Bevan's gesture regarding the salary question, but many of us are still perturbed by other points which have not been satisfactorily settled. It is difficult to see how a simple plebiscite could possibly express the detailed views of the profession on those points still at issue. I venture to put my own views, held for some time, and which I feel are minimum requirements to satisfy our difficulties in agreeing to enter the Service.

(1) I have always opposed the insistence on the right of appeal to the courts against dismissal, since such action could be ruinously expensive in time, money, and reputation to the doctor concerned. Far preferable is the right of appeal to the Tribunal envisaged in the Act, provided that such a Tribunal were appointed by the Lord Chancellor and in no way by the employing authority.

(2) The retention of goodwill of practices is not a question of finance but has as its fundamental object the freedom of the profession. Unfortunately this issue has become a matter of emotion rather than good sense and the public and all political parties appear equally opposed to its retention. In view of this I feel that doctors might give up the goodwill of practices provided that the Act were amended to safeguard certain essential freedoms and to facilitate partnership and group practice arrangements.

(*a*) A doctor must have the right to select at his own discretion a partner, assistant, or locumtenent on terms mutually agreed.

(*b*) The payment of adequate compensation at the time for that proportion of a practice income transferred to an incoming partner.

(*c*) The payment of adequate compensation on death, retirement, or removal from one area to another.

(*d*) The removal from the Act of the power of negative direction, since the closing of certain areas to new entrants would nullify the freedoms envisaged in the foregoing clauses.

The points expressed in this letter could in no way diminish the objectives of the National Health Service Act but if conceded might well achieve the good will of the medical profession. Anything less than a whole-hearted co-operation by the doctors would be a disaster to the Health Service envisaged for the nation.—I am, etc.,

Taunton. R. D. ROWLANDS.

A Bad Service

SIR,—Once again the Presidents of the Royal Colleges, failing to learn from the unhappy results of their previous intervention, have superseded the Negotiating Committee in its dealings with the Minister. They have given to the public the erroneous impression that they are armed with a mandate from the whole profession. The positive result of this is that the Minister has seized the "face-saving" opening for which he has been sparring in order to make a concession to the doctors. He has given way on one principle only among those upon which we took our firm stand. The song and dance which has resulted in the lay press points to the negative result of this second stab in the back. If we continue to decline to work the Service we will receive a bad press and incur the hostility of our patients.

In point of fact we are very little further advanced towards the achievement of our minimum standard than we were before. This remains a bad service from the point of view of the public. Even if we doctors agree to work it, where are the nurses, the hospital beds, the health centres? From the doctors' standpoint where are the secretaries and receptionists needed to replace our hard-worked wives, who rightly have no intention of acting as unpaid slaves for the Minister? In what way does our remuneration coincide with the recommendations of the Spens Committee? Will the Government pay us rent for the use of our surgery accommodation, having postponed indefinitely the building of the promised health centres? Why should we not retain the ownership of our practices? Take that away and our incentive to keenness and enthusiasm goes with it. These and several other points require a satisfactory answer before we should agree to enter the Service. Meanwhile, let us hope that the Presidents have not damaged our case irreparably with the public. Here, indeed, is an urgent job for the Public Relations Officer.

By all means let us have our service; but let it be one which the country in its present dire straits can afford. Let it be introduced a step at a time until we have the first-class service which we all desire. And meanwhile let our Negotiating Committee stand firm at the line upon which they received the mandate of the profession at the recent plebiscite.—I am, etc.,

East Horsley, Surrey. BASIL S. GRANT.

Special Procedure

SIR,—From the general practice standpoint I should not be happy to see Regulations "vetted" by a Parliamentary Committee. We as a profession know far more about the N.H.S. Act than 20 Parliamentarians who are, or should be, interested in all the Acts they have framed. In addition to this we can realize at once the effect of a regulation on practice. The I.A.C. or its successor is the best body to "vet" new regulations as they affect general practice. A renewed assurance that regulations affecting general practice should be sent to the Association's Committee within whose terms of reference they naturally fall, and a similar assurance for consultants, would in my view meet the case without any further committees.—I am, etc.,

Solihull, Warwicks. ARTHUR BEAUCHAMP.

Ownership of Goodwill

SIR,—Mr. Bevan's latest "concessions" are a clever move designed to split the profession. Actually he has given away very little, and there is nothing to prevent his introducing a Bill at any time to make the Service a whole-time salaried one in spite of all his assurances. To my mind, the ownership of our goodwill is the essential thing; if we lose that, we have nothing.

There are those among us who strongly believe that within ten years there will be so many of the public dissatisfied with the National Health Service that a considerable number of doctors will be leaving the Service to do private work only. I feel also that a great many doctors will be sadly disillusioned over their compensation when it comes to be worked out. Some members of our profession who have already had experience of Government contract service know how the doctors' work will be interfered with right, left, and centre by non-medical people.

Let us stick solidly by the B.M.A. no matter what the result of the plebiscite, and have faith in our patients and the public: we can trust them more than the politicians. United we stand, divided we fall. Don't let us ever forget that. There will be much work for the B.M.A. to do during the next few months no matter how the plebiscite goes, and we must have unity if we are to achieve anything of lasting value.—I am, etc.,

Burton-on-Trent. J. R. SALMOND.

Cat-and-Mouse Game

SIR,—Whatever the outcome of the plebiscite now being conducted, I feel, and I am sure many feel as I do, that the action of the Council of the B.M.A. merits very severe condemnation.

Mr. Bevan had hardly regained his breath after his speech in the House of Commons on the National Health Service when the B.M.A. Council seemed to have developed hysteria and summoned an emergency meeting, and it was not long after that

their chosen spokesmen were waiting, cap in hand as it were, to see what tit-bits they could extract from the Minister. Why the hurry on their part? The Minister knew our terms and he was not prepared to yield and defiantly stated that the Health Service would start on the appointed day whatever our feelings. We as a profession had expressed in no uncertain terms our unwillingness to accept service under the Act as it then stood at the time of the last plebiscite, and the Council of the B.M.A. had undertaken to respect the vote of the profession. It therefore had no authority from the profession to meet the Minister and reopen the subject. By doing so the Council, in my opinion, has committed a serious breach of faith, and furthermore the profession has been held up to ridicule and our case has been weakened.

I am a staunch supporter, Sir, of all the principles for which the B.M.A. has been fighting, but at the same time I can recognize and condemn weakness; and it is not likely that I, or those who feel as I do, will be prepared to part with £100 for the privilege of standing outside the arena to watch this "cat-and-mouse" game. It's got to be all or nothing, and unless we adopt this attitude it is worthless making a mock attempt to fight for principles.

The eyes of the rest of the world are focused on us. Medicine throughout the universe will either sink or swim according to the strength of our efforts in this struggle. We try to pride ourselves on being the "guiding-star" in the field of medicine, but we cannot uphold this reputation unless we make a very determined and unflinching stand in the interests of a profession which throughout the ages has had the confidence of man. If we have not the courage to do this on our own behalf, let us do it on behalf of the man and woman who trust us to protect their lives and interests.—I am, etc.,

London, W.1. E. S. FENNELL.

Unsolved Problems

SIR,—*Ownership of the Family Doctor's Practice.*—The Socialist Party have declared their determination to abolish the right of a doctor to own his practice and are determined to buy him out at great public expense. Their spokesmen have given three reasons for this, two of which are untrue, the third quite irrelevant. (1) "In no other country do doctors buy and sell the goodwill which they have built up in their practice." This is untrue. In many countries, including Belgium and Holland, the introduction to an accumulated practice is by purchase. (2) "Even the Conservative Party would not agree to the retention of the right to sell goodwill." The Conservative Party have never published any policy to this effect. Indeed, in a "property-owning Democracy" doctors should be encouraged to own their own practices. (3) "With doctors remunerated by public funds it would be unthinkable for a practice to be sold." This is quite irrelevant, as the patients would be accumulated as personal patients of the doctor.

What then is the system the Socialists have invented to replace the old pattern of natural supply and demand? It is this: that committee rule will prevail and doctors will be prevented from going into areas which are "over-doctored." This is a fantastic solution, as it cannot rectify the main difficulty which it is supposed to correct—i.e., that a few areas are in fact under-doctored.

Doctors cannot in any case go into adequately doctored areas and make a living without (1) buying a part or whole of a practice, or (2) securing a salary as an assistant, or (3) spending any capital they have at their command in building up a practice. No doctor would buy a practice in an under-doctored area, for there he would "squat" and build one up quickly. And how doctors in the new Service will be appointed to the best or least desirable practices no one knows. In this "paper" service the essential details are quite unworked out and unworkable.

The Doctor's House.—This is another unsolved problem. The outgoing doctor not being allowed to sell his practice, it is highly improbable that the incoming doctor will succeed to the house and surgery, for if he sold his house at the present market value to another doctor at a price deemed to include sale of goodwill he could be fined or imprisoned, or both, under Sect. 34, N.H.S. Act, 1946. Obviously a non-medical purchaser must be found and the house lost to medical practice. Where will the incoming doctor get a house in these days of acute housing shortage?

Mr. Aneurin Bevan has thought that the doctors' "unease and restlessness" could be banished by some minor adjustment in the payments of basic salary and capitation fee. How little does he grasp the deep objection of the medical profession to being forced either into a State medical service or a whole-time State salaried service. Tradition and experience attach doctors to their patients. It will be increasingly difficult to be loyal to their patients with State interference at every level by daily increasing highly paid bureaucrats.—We are, etc.,

E. T. WRIGHT.
London, W.1. G. H. ROSSDALE.

Events in Czechoslovakia

SIR,—I am sure we all feel saddened and disturbed about the turn of events in Czechoslovakia and their reflection in the boycott by the British of the centenary celebrations of the Charles University, but we do want our friends in that country, especially in Prague, to realize our real sentiments of good will and regard towards them. Possibly the *British Medical Journal* may be a means of communication that can take the place of so many avenues that are closed. Those of us who were to receive honorary degrees or to act as official representatives of universities or other learned bodies were bitterly disappointed to have to deny ourselves the privilege of attending as an act of homage to so ancient a seat of learning. To have done so would have been to condone the new stifling regime with its suppressions and frustrations. There is also another reason which I have not seen mentioned: to have been present and to have warmly recognized our friends would have been natural but might have brought suspicion or official disapproval upon them, while studied neglect on our part as a policy of safety might have been misunderstood and might have offended them deeply. In the dilemma it seemed best from all points of view to stay away, much as it was to be regretted.—I am, etc.,

Taplow, Bucks. G. GREY TURNER.

Medical Photography

SIR,—Most workers in the laboratories and other ancillary departments of hospitals would agree that Dr. Ffrangcon Roberts (March 13, p. 485) has not in any way exaggerated the increasing demands on their services, nor minimized the relatively little contribution to the beneficial treatment of the patients which such demands have produced. I have recorded elsewhere (*Brit. J. Radiol.*, 1945, **18**, 249) the main abuses of radiology, but apparently only inordinate boosting of his specialty by the expert (which will the more readily bring it into disrepute) can achieve any appreciable effect.

Though, as Dr. Roberts has shown, there has been a general increase in the demands for some years, since the end of the fighting of World War II, and more particularly since the Minister of Health announced his intention of taking over the hospitals, the full-time personnel and the expenditure of the larger hospitals, aided by their priorities, have increased considerably, but nothing to what they would have done had the services, goods, accommodation, and funds been more readily available.

With 42 years' experience in medical photography I do not share Dr. R. G. W. Ollerenshaw's views (March 27, p. 618) on it. "Doing it the hard way," as I could show, we were able to make as good illustrations 40 years ago as we can to-day, and I doubt very much whether the present facilities which permit of easier production will do any more than excite extravagant expenditure of material and time. True, much of the medical photography in the past was done at the expense of the interested clinician—a very useful corrective which I see no excuse in departing from.

Dr. Ollerenshaw admits that "it is quite certain that the demands of teachers for the products of the department are wellnigh overwhelming in spite of expansion," but is not this claim "for teaching purposes" being overdone? Have we not excellent illustrations in the literature of all the more common conditions? The rarities, though most interesting, are infinite, but of little use for teaching purposes. We have the optical facilities for projecting or reproducing any illustrations. He states that improvement in the standard of pictorial and line work submitted to the journals for publication is much needed. But surely in these days of high quality production this is a reflection on the efficiency of the editorial boards.

I find in present case histories, and indeed in the literature, illustrations which are not wanting in quality, but their legends and descriptions sometimes are lacking in accuracy, apparently because the condition illustrated is ill-understood. Included in a large number of cases in a series, illustrations of conditions are recorded which are not of the series, and often it is this erroneously included illustration which is chosen for resemblance by other writers adding to the series. Very few of the multitudinous photographs possessed by those who have shown enthusiasm for medical photography are put to any general use. Good as they are and interesting to the particular observer, he is given little chance of using them, and, as photographs are made to show the features the interested observer wishes, only he may appreciate their value and what they were made to show. It is said that the photograph cannot lie, but those who understand their possibilities, even with the cinema, know that a very false impression can be created, though it was neither designed nor wished.

How many of the teaching cinema films indicate to the student the difficulties of their productions, quite apart from the photography? The film may appear to indicate a skill, dexterity, or result far different from the actual. The very simplicity of a procedure in skilled hands may entice the novice to try his hand. With such education and practice the novice in sculpture would not be allowed to maltreat a piece of marble.

Medical photography results in the accumulation of material which can be of little material value. Like the snapshots of the amateur they become so numerous as time goes on that they fill every available space, and only removal or death secures their destruction. While writing this letter I have received a hospital report which records under this heading, "It is interesting to make comparison with previous years:

1945	1,119	negatives	4,506	prints
1946	3,360	„	6,996	„
1947	4,958	„	10,652	„ "

What a magnificent increase! For what?—I am, etc.,

Edgbaston, Birmingham. JAMES F. BRAILSFORD.

Health of Students

SIR,—Dr. Emily A. C. Wilson (April 10, p. 708) was puzzled about the conclusion in my article (March 13, p. 490) on "The Health of 407 New Students" with regard to previous dental treatment: "It seems probable that financial considerations had prevented some of the students from the poorer social groups from obtaining dental treatment."

It would not be correct to assume, as I think Dr. Wilson does, that students entering a university in October, 1946, had all had free dental inspection and treatment offered them in their secondary schools. In the report of the Chief Medical Officer of the Ministry of Education for the year 1939–45[1] it is stated that "under the Education Act of 1921, relatively little was done to provide dental treatment for secondary school pupils." The Education Act of 1944, which was not implemented until April, 1945, obliges local authorities to provide dental treatment facilities for secondary school children, but owing to the call-up of school dental officers during the war, which in some areas amounted to half the dental staff, there are still secondary schools which have not yet been visited.

Mr. Sidney Pappworth (April 3, p. 663) finds it difficult to believe that 16% of the Sheffield freshmen had postural defects of the spine, yet Parnell[2] found an incidence of 28% in a group of Oxford students. In asking for controls he perhaps misunderstood the purpose of my survey, which was to describe the health of a group of university students with a view to discovering the health needs of this group. No attempt was made to show that their state of health differed from that of non-students of a similar age, and therefore no control series was necessary.

Dr. F. J. Kelleher (March 27, p. 617) objects to my psychiatric terminology. The term "marked introversion" conveys, I believe, to the ordinary medical reader the type of person meant, and "nervous breakdown" referred to a recent *history* of this condition, as the text of the article indicates. It would have been wrong, I think, for a non-psychiatrist to have attempted to translate that expression into an "accepted psychiatric syndrome." The students were not subjected to the Rorschach or other psychiatric test. As your leading article (March 13, p. 504) states, special mental health examinations have been tried in one university in the United States of America, but were discontinued as it was found that "results failed to justify the additional organization, work, and cost." The physician in charge of a student health scheme certainly needs the assistance of a psychiatrist in the diagnosis and treatment of the more severe cases of mental ill-health, which, as you state, are not rare. He also needs the help of an orthopaedic surgeon, oto-rhino-laryngologist, dermatologist, and other specialists for the treatment of established illness in students. In the University of Sheffield students' health service we have been fortunate in receiving much valued help of this kind from the consultant staffs of the Royal Sheffield Infirmary and Hospital.

Those who have not themselves had the opportunity of carrying out routine health examinations on unselected population groups are often surprised at the high incidence of defects and disorders reported in surveys of this sort. Morris,[3] for example, examined 1,592 workers in a Midlands corporation and found that 7% had a major disorder, and that minor disorders such as "bad teeth, dyspepsia, hernia, chronic bronchitis, defects of hearing and vision, anaemia, varicose veins, and deformed feet were legion." Pearse and Crocker[4] found that of the members of the Peckham Health Centre only 4% of the women and 14% of the men could be classed as free from disorder. Parnell's findings in examining a group of university students included 33% with myopia, 32% with skin lesions, 15% with ear, nose, and throat conditions, and 13% with minor anxieties. At routine health examinations illnesses such as hypochromic anaemia and pulmonary tuberculosis can be detected at an early and usually curable stage. At the same time deviations from the average, such as symptomless flat foot or transient systolic hypertension, are discovered, the significance of which is not yet fully understood. By following up individuals showing deviations of this sort it should be possible to determine which signs can be regarded as normal variations and which constitute the earliest evidence of disabling illness such as essential hypertension, peptic ulcer, and neurotic or psychotic breakdown. Possibilities in the prevention of the development of these illnesses might then emerge.—I am, etc.,

University of Sheffield. JOHN PEMBERTON.

REFERENCES

1 *The Health of the School Child*. London: H.M.S.O. 1947.
2 *Lancet*, 1947, **2**, 939.
3 Ibid., 1941, **1**, 51.
4 *The Peckham Experiment*. London. 1944.

Disk Lesions and Osteopathy

SIR,—Dr. James Cyriax (April 17, p. 754) has completely missed the point of my letter in reply to Dr. Craig and Mr. Lipmann-Kessel's letter. It was not my intention to draw an analogy between the osteopathic theory and protrusion of an intervertebral disk. Quite the contrary.

In order to make my point clear let me quote more extensively from Dr. Craig and Mr. Lipmann-Kessel's letter. They said, "It is generally accepted that on clinical evidence alone the level of a lumbar spine disk lesion cannot be confidently predicted. It may be that the present conception of sciatic pain as the result of root compression is responsible for this difficulty, and if it were regarded as a deep segmental pain due to joint disturbance this difficulty might be resolved. Over-simplified views of the pain mechanism in this condition are liable to follow a mechanical interpretation of the functions of the central nervous system."

While not denying that gross protrusion of an intervertebral disk accounts for a small proportion of cases of sciatica this broader conception of the probable underlying pathology not only of the majority of cases of sciatica but of many other conditions as well is exactly what has been suggested by the osteopaths for many years now. I repeat, in my opinion there is more truth in the osteopathic conception that has hitherto been admitted by the orthodox medical profession.

Many of Andrew Taylor Still's contentions have and will continue to be modified in the light of progressive knowledge, but this in no way detracts from his great contribution to medical progress. Certainly the modern conception of circulation differs considerably from that enunciated by Harvey, but he is nevertheless universally acclaimed the discoverer of the circulation of the blood.—I am, etc.,

London, W.1. GEORGE MACDONALD.

Intra-abdominal and Intrauterine Pressures

SIR,—In his interesting dissertation on the mechanics of egg-laying (March 27, p. 585) Prof. H. A. Harris accepts the calculation by Haughton[1] of the maximum human intrauterine pressure during parturition. This reverend scientist was not, however, always near the mark with his calculations, as is shown by his figure for the maximum intra-abdominal pressure. From

measurements of the thickness of the muscles in the abdominal wall, the curvature of the linea alba, and the absolute muscle force, or maximum force per unit of cross section of the fibres, he arrived at the impressively exact figure of 32.926 lb. per sq. in. (1702 mm. Hg). The figure for the absolute muscle force which he used was 102.55 lb. per sq. in. (7.21 kg. sq. cm.), and this is nearly double my own figure,[2] which took into consideration many more factors.

Allowing for this discrepancy, however, Haughton's figure for the intra-abdominal pressure would still be many times greater than the systolic blood pressure. If this were actually the case the blood flow in the lower limbs would cease completely during periods of high abdominal tension. But a simple observation that the pulses at the ankles are still present during severe abdominal straining indicates that the intra-abdominal pressure must be less than the systolic pressure. This is confirmed by measurements which I made some years ago by introducing a balloon, connected to a manometer, through the opened sac of an inguinal hernia exposed under local anaesthesia, and then with a swab pressed firmly over the inguinal canal encouraging the patient to strain down with maximum effort. The best two readings in six cases were 75 and 80 mm. of Hg, and there was no doubt that these young men were trying hard. Barcroft and Millen[3] have shown that the tension within a voluntary muscle at maximum effort can be high enough to stop its blood flow, but from the above readings it is apparent that the maximum intra-abdominal pressure is well below the normal systolic level.

It seems likely that this applies also to the maximum intra-uterine pressure, since a pressure greater than systolic levels would cut off the flow of maternal blood through the placenta and would arrest the foetal circulation. The figure of 3.4 lb. per sq. in. arrived at in Haughton's calculations is therefore likely to be well above the actual maximum pressure. His work illustrates well the fallacies which may result from inductive reasoning applied to body functions—the only way to get at the truth is to "try the experiment."—I am, etc.,

Manchester. H. A. HAXTON.

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1 Haughton, S. (1873). *Principles of Animal Mechanics*, London.
2 Haxton, H. A. (1944). *J. Physiol.*, **103**, 267.
3 Barcroft, H., and Millen, J. L. E. (1939). *Ibid.*, **97**, 17.

Prompt Publication

SIR,—I have always had the greatest admiration for the department of the B.M.A. which is responsible for the publication of the specialist quarterly journals, but recently this department has quite excelled itself. In the issue of the *Journal of Neurology, Neurosurgery, and Psychiatry* dated November, 1947, there appears a long and valuable article which was received at the editorial office on Nov. 29, 1947. Such an achievement demands and must receive the warmest congratulations. As the journal cannot be expected merely to rest on its laurels in the future and must like all of us "raise its sights," I suppose that we can confidently look forward to the time when it will be publishing articles some months before they are written.—I am, etc.,

London W.1. SAMSON WRIGHT.

The Problem of Caries

SIR,—Your annotation (April 10, p. 697) on this subject requires some clarification and correction. Does the writer maintain that caries does not, or that it need not, involve decalcification, or merely that it is not purely and simply decalcification? Or does he mean that proteolysis may or does precede decalcification either in enamel or dentine? What conception is it that recent work has shown to be untrue, and what decalcification hypothesis is it that Dr. P. Pincus has "shattered" with his earlier work?

The chemico-parasitic theory was not originally deduced from a "belief," but from observation of now well-known facts, and it has since been amply confirmed by nearly all the work that has been done on the aetiology and prevention of caries. Frisbie's theory, which you refer to, depends on his observation[1] that some alteration of enamel occurs while its natural surface, and the surface of ground sections, is still "essentially hard in the physical sense. Examination by means of instruments may or may not reveal a roughened or irregular surface." This vaguely described observation seems to be his only reason for supposing that no decalcification had occurred. However, Applebaum[2] has shown that carious enamel becomes radiolucent to Grenz rays before its surface continuity is lost and while it is still hard enough for the preparation of ground sections. This clearly indicates that decalcification has begun at that very early stage.

The earlier paper of Pincus,[3] which is cited, does not specifically describe any destruction of the hard part of the enamel but merely some alteration in the surface of teeth which seem from the illustrations to be still covered with Nasmyth's' membrane or the remains of the enamel organ. It is not stated how long the teeth had been erupted or whether they had erupted at all. No sections are described or illustrated, and the author only claims that the appearance suggests that "some of the enamel was disintegrated . . ." Few would agree with him, unless by "some of the enamel" he means only the organic matter lying on or at the surface of newly erupted or unerupted enamel. He makes no claim to have shattered any hypothesis, and the real value of his work as dental research is, I suggest, that after years of painstaking effort he has *not* been able to produce anything resembling caries in the absence of acid or acidogenic bacteria. Artificial or *in vitro* caries with acid-forming bacteria has of course been known for many years.

Perhaps the writer of the annotation was misled by the statement of Dr. Pincus, in his discussion of caries, that dentine is 23% organic matter. Enamel, where caries usually begins, has a much lower content—usually reckoned as about 2%. It has long been realized that proteolysis is an essential part of dentine caries, but there is still nothing to suggest that it is essential or important in the caries of enamel.

A glance at any number of the *Journal of Dental Research* will show that the theories of Pincus and Frisbie are not as your annotator suggests widely accepted by research workers in the U.S.A.; and his own views go even beyond the unorthodox theories of those two workers. The last paragraph of the annotation is also very puzzling. Why does caries occur at stagnation areas if stagnation areas are caused by caries? Surely it would be better if comment in the *Journal* on Pincus's theory was made from a more orthodox or impartial viewpoint, or at least that such extreme and obscure theories should not be presented as though they were generally accepted?—I am, etc.,

London, N.W.6. R. B. D. STOCKER.

REFERENCES

1 *J. dent. Res.*, 1947, **26**, 181.
2 *Dental Cosmos*, 1935, **77**, 931.
3 *Brit. dent. J.*, 1937, **63**, 511.

SIR,—I read with interest and some surprise in the annotation (April 10, p. 697) on this subject that "many dental research workers still refer to dental caries as a process of decalcification"; that "recent work . . . indicates that this conception is far from the truth"; and that "it is on such lines that much of the research work on caries is now being done in the U.S.A."

I have just returned from a five-and-a-half-months tour of research centres in New York, Ann Arbor, Mich., Rochester, N.Y., Minneapolis, Indianapolis, and others, for the express purpose of discovering the views of the research workers upon dental caries and its prevention. My impression is that the conclusions of the overwhelming majority of these men are diametrically opposed to the views expressed in your annotation, and that notwithstanding much research upon proteolysis.

I quote the findings of that large body of research workers known as the "Michigan Workshop," whose 25th meeting was held from Sept. 8–13, 1947, as published in the *Journal of the American Dental Association* (1948, **36**, 4): "Dental caries is a disease of the calcified tissues of the teeth. It is caused by acid resulting from the action of micro-organisms on carbohydrates, is characterized by a decalcification of the inorganic portions, and is accompanied or followed by a disintegration of the organic substance of the tooth."

Fosdick, Professor of Chemistry at the North Western University, states in the *New York Journal of Dentistry* (1947, **17**, 55), "Recent research in dental caries has primarily emphasized the early position of Miller and Black, in that the condition is an acid decalcification of the inorganic structure of the teeth accompanied or followed by a putrefaction of the organic portions."

Volker, in the *Journal of the New Jersey State Dental Society* (September, 1947), says, "In conclusion it may be reiterated that our present knowledge of dental caries supports the view that we are:

dealing with an environmental process in which three factors, retained fermentable carbohydrates, acidogenic bacteria, and the enamel surface play the leading roles."

It is true that certain writers, notably Prof. Gottlieb, believe that proteolysis is of major importance in the initiation of dental caries, but it is my experience that these men find few sympathizers among the research workers in the U.S.A.

Dr. Pincus's interesting and valuable contribution in your same issue throws further light on the role of proteolysis in the progressive increase of a cavity when once formed. As one interested in the prevention of dental disease, the question as to whether the primary breach in the enamel of the tooth is due to proteolytic or acid-forming organisms is of far more than academic interest.—I am, etc.,

London, S.E.1. GILBERT J. PARFITT.

Aluminium Pneumoconiosis

SIR,—In the annotation (March 13, p. 506) you have a comment on aluminium pneumoconiosis. This write-up is very interesting. I would like, however, to correct a rather doubtful statement made therein. The article states, "The Canadian investigators think that the disease may be a form of silicosis caused by vaporized silica." Just what your authority for this statement is, is difficult to see. We have always been conscious that, in the presence of so much silica, silica as a possible cause or contributing cause of the condition found in the abrasive workers could not be overlooked. We do not, however, feel that this is modified silicosis. We incline to the opinion that the disease is produced by the extremely heavy exposure to alumina. It is realized that as yet we have not complete evidence that this opinion is correct. Some experimental work is being done which may resolve the problem.

It would be interesting if you canvass the situation in regard to an aluminium plant in Sweden. Dr. Sven Forssman, Professor of Industrial Hygiene, State Institute of Public Health, Tomteboda (near Stockholm), Sweden, showed me two lantern slides from films prepared on men who had been employed in the plant concerned. The lung changes exhibited by these slides were very similar to those found in our abrasive workers.—I am, etc.,

Division of Industrial Health,
Department of Health,
Toronto, Ontario. A. R. RIDDELL.

Medicine and the Arts

SIR,—Prof. Geoffrey Jefferson is too sweeping. In the course of a reply (April 10, p. 705) to a scientific correspondent he makes a brief excursion into the arts, and in half-a-dozen lines disposes of Elizabethan prose and the writers of long poems. He writes, "The art of tight and lucid compression of thinking was unknown in Bacon's day." Surely Bacon, on the contrary, was the earliest English exponent of the aphorism, the essence of which is conciseness. In his *Advancement of Learning* he distinguishes two methods of writing, by formal discourse or by aphorism. One method or the other was to be adopted—they could hardly be combined—and therefore he practised both. The difficulty of reconciling comprehensiveness with brevity is an old one.

From prose to poetry, and the professor's faith in Baudelaire's dictum, "Long poems were written by those who had not the talent to compose short ones." This can hardly be dismissed with a smile as an exaggeration, because it is not the exaggeration of a truth. Rather is it a Gallic *bon mot*, not to be taken too literally; perhaps Baudelaire was a better poet than critic. Be that as it may, the English Muse refutes him wherever the pages are turned, even in Lancashire. One example will serve to counter Baudelaire's thrust and display our poets' mastery of both forms, the long and the short—that superb short poem "The Poppy" with its opening stanza,

> "Summer set lip to Earth's bosom bare,
> And left the flush'd print in a poppy there;
> Like a yawn of fire from the grass it came,
> And the fanning wind puff'd it to flapping flame."

The poet was Francis Thompson, one-time student of the Manchester Medical School (1877–83), who was capable, too, of sustained inspiration in his long poem, "The Hound of Heaven."—I am, etc.,

Ashton-under-Lyne. F. G. RALPHS.

Bone Conduction in Otosclerosis

SIR,—It is interesting to note the contradictory opinions expressed by the commentators on my letter printed in the *Journal* of March 20 (p. 569). Mr. R. Scott Stevenson (March 27, p. 618), quoting the work of Tumarkin, refers to "the myth of increased bone conduction" in otosclerosis. Mr. R. R. Woods (April 17, p. 754), while referring to the genuine improvement of bone conduction which occurs in the operated ear (after the fenestration operation), goes on to say that he has never seen the hearing of the unoperated ear altered in any way, either for air or bone conduction; indeed, he says it is inconceivable that an operation on one ear could affect the working of the opposite one. Mr. E. R. Garnett Passe (April 17, p. 754) writes, "It has been known for some time now that improvement to hearing by both air and bone conduction occurs in the unoperated ear in a certain number of cases, but this improvement is never permanent."

The case I referred to illustrated the fact that increase in air and bone conduction can occur in the unoperated ear, and I made no claim whatsoever to a permanent result for this case. In February, 1947, Mr. Passe published in the *Lancet* the results of one hundred fenestration operations done by the Lempert technique since August, 1945. With an equal operative experience to this number over the last two years, and with an operative technique which the results substantiate, I hope I can give equally well what he and Mr. Scott Stevenson call a "careful, sober, and dispassionate estimation of end-results."—I am, etc.,

London, W.1. W. H. B. MAGAURAN.

Transfusion Reactions

SIR,—Dr. John Wallace and Mr. R. D. Richards in their article (April 3, p. 640) on transfusion reactions describe cases in which venous spasm interfered with infusion of red cells. I have seen a reaction to infusion closely resembling the case described in detail in the article, where venous spasm also seemed to be the cause. Other evidence, however, suggests a different explanation. The recipient was a healthy nurse belonging to Group A. She was given 500 ml. of Group O blood in order to estimate survival of the donor's red cells in a normal person. Venipuncture was performed apparently satisfactorily, and the infusion ran quite freely. Some thirty minutes after the transfusion began the recipient complained of a little aching in the arm, and when nearly 400 ml. had run in the pain became more severe. It was now noticed that there was acute tenderness and swelling localized to the biceps. The infusion, however, was still running quite freely, but was stopped in view of the discomfort.

In estimating the survival of the Group O blood, using the method described by Ashby in 1919, as modified by Dacie and Mollison in 1943, it was found that no increase in the number of inagglutinable cells (Group O cells) had occurred after the transfusion was stopped. From this it was inferred that none of the infused cells had reached the general circulation. Swelling of the biceps was followed by discoloration of the skin of the lower arm and upper forearm. Full recovery of function in the arm and subsidence of the swelling took place in about ten days.

From these observations it seems likely that the blood was infused into the intramuscular spaces in the biceps due to the intravenous needle passing through the vein into the muscle, and that venous spasm was not the true explanation of the reaction.—I am, etc.,

Manchester. W. K. STEVENSON MOORE.

A Case of White Asphyxia

SIR,—It is still no exaggeration to say that many theatres in the country are not equipped for this emergency and, what is more, there is much scepticism regarding the efficacy of cardiac massage. Various claims have been made as to the period of cardiac arrest from which recovery has taken place, but the average time limit is five minutes. The central nervous system can tolerate total arrest for three minutes ten seconds, and even then there is some permanent alteration in psychic behaviour.

On Dec. 18, 1944, a man aged 68 underwent partial cystectomy under light spinal "nupercaine" and light general anaesthesia. While the abdominal wound was being closed the anaesthetist reported that the patient had stopped breathing. On examination his was a typical case of white asphyxia. By the time cardiac massage was started through an upper abdominal incision three to four minutes must have elapsed. He was given nikethamide, and artificial respiration was commenced at the same time. Cardiac massage had been carried out for about two minutes when the heart started beating again. Some adrenaline was injected into the heart muscle. The patient was returned to the ward, and by slow drip one pint (568 ml.) of blood was given, along with an intramuscular injection of suprarenal cortex extract. The patient was still in deep coma at 9 p.m. The night nurse reported: "Patient seems to be semi-conscious, but is very dazed." In the morning to my great surprise he was semi-conscious and irrational. He was restless for a few days, and from Jan. 1, 1945, his condition improved. On Jan. 3 he was fully conscious, but on the 4th he again became restless, and was not able to pass urine. Two stitches were removed from the suprapubic wound and a large blood clot taken away. Next day, as he did not improve, the suprapubic wound was reopened under local analgesia and intravenous "pentothal," a blood clot removed, the bladder washed out, and a suprapubic drain put in. Progress was satisfactory until Jan. 12, when the upper abdominal wound burst open, with protrusion of omentum. Under local and regional analgesia the abdominal wall was resutured. Progress was uneventful, and he was discharged fit, passing urine normally. He was sent to see Dr. F. M. R. Walshe and Dr. Parkinson. Both reported no organic changes as a result of the asphyxia. When last seen he was fit and active.

The unusual features of this case are that the patient was able to stand two further surgical manipulations under pentothal and local analgesia so soon after his recovery. Though I have seen further examples of cardiac arrest which have not turned out so favourably I have become a firm believer in this life-saving measure. My own view is that for the measure to be more uniformly successful one must start the massage as promptly as feasible and in perfect confidence.

I wish to thank Mr. Harold Dodd for permission to publish this case.—I am, etc.,

Swansea General and Eye Hospital. SUNDRAM PILLAI.

POINTS FROM LETTERS

Prickly Heat

Colonel T. C. RUSSELL ARCHER, late R.A.M.C., writes: Correspondence on the treatment of prickly heat has prompted me to forward the undermentioned formula for my colleagues in tropical practice: Salicylic acid, 3 parts; perchloride of mercury, 0.1 part; industrial methylated spirit to 100 parts. This formula was used by me with considerable success when serving with the West African Expeditionary Force in the Far East, but on reflection I feel it would be much improved by the addition of 70% alcohol in place of methylated spirits.

The Design of Bed-pans

"Professional Victim" writes: Having recently undergone a major operation I was much interested in Mr. Malcolm Donaldson's letter (March 27, p. 618) on the above subject. A doctor who had been wounded wrote to the *British Medical Journal* about it during the war. He pointed out that the bed-pan hinders defaecation by pressing the buttocks together. The lavatory seat, on the other hand, helps it by separating them and putting the anus on the stretch. . . . A bed-pan of a shape approximating to the lavatory seat might be clumsy for the nurses, but I believe it would reduce the discomfort of our patients enough to be worth the extra trouble involved.

Herpes Zoster and Chicken-pox

Dr. ERNEST SOYSA (Colombo, Ceylon) writes: The following cases may be of interest in reference to Dr. C. C. H. Chavasse's observations (Feb. 14, p. 318) on the association of herpes zoster and chicken-pox. On Jan. 19, 1948, a mother aged 40 took her daughter aged 13 to a doctor in whose household there had been several cases of chicken-pox during the preceding three months. On Jan. 28 the mother complained of pain in the right eye and supra-orbital region. The next day a few small vesicles appeared above the right eyebrow. By Feb. 1 a severe herpetic rash had spread over the right supra-orbital region, with acute frontal neuralgia, swelling, itching, lacrimation, and vomiting. The condition began to improve after a week. The pain subsided gradually, and the herpes cleared up leaving severe scarring of the right side of the forehead. On Feb. 14 the patient's daughter developed an attack of chicken-pox which was mild and subsided within ten days, leaving little scarring. On March 1 a maidservant who had looked after the last two patients also fell ill with chicken-pox and made an uneventful recovery.

Clothing Coupons for Colostomy

Mr. J. C. GOLIGHER (London, W.1) writes: It is not perhaps generally appreciated in the medical profession that additional clothing coupons may be claimed by patients with colostomies or ileostomies in order to cover the purchase of a suitable belt and the extra underwear, bed linen, etc., made necessary by their condition. . . . Patients should write to the Board of Trade (Invalid and Medical Section), 91, Victoria Street, S.W.1, and ask for Form P.C.128, on which the application should be made. A supporting medical certificate from the doctor or surgeon is also necessary. In completing the form it is important to state that the application is made in respect of both an appliance and extra clothing, otherwise only three coupons, just sufficient to buy a belt, will be sent. If the need for additional clothing is also mentioned, the allowance granted is 30 coupons. This is, of course, a yearly allocation and a fresh application should be made annually.

Sweet Urine Containers

Dr. P. E. FITZPATRICK (Belfast) writes: Dr. W. E. McCulloch's point (March 27, p. 620) interested me greatly, for it shows how a doctor can be completely taken in. About a year ago I had a patient who had been complaining of various nervous symptoms—paraesthesia, polyuria, etc.—and on clinical examination I could find no signs of any organic disease. As is my custom I asked for a specimen of morning urine, and I was extremely surprised to find it was full of glucose. Accordingly I referred my patient to a specialist for a blood-sugar estimation, etc., and imagine my surprise when I was informed that the blood sugar was normal and the urine was free from sugar. I did a further test and this time the urine was sugar-free. Accordingly I made a successful search for the bottle which contained the original sample (three days later), and examined it again. It showed glucose ++++. Fortunately the label of the chemist was on the bottle with the code marking. I inquired of the chemist what had been in the bottle and he was able to inform me "glycerine and honey." Fortunately I had not informed my patient about the glycosuria, and she is now completely well, with no symptoms. The moral, I think, is obvious.

Asthma and the Inhaler

Dr. DENIS DOOLEY (London, W.C.2) writes: May I endorse the remarks of Dr. A. W. Paterson (March 20, p. 573)? For a long time I have prescribed a bronchovydrin type of inhalant for patients with asthma and am highly satisfied with the results. I suggest that the damage to the cilia as mentioned by Dr. Clement Francis (Jan. 10, p. 76) is caused by the acid in some of these inhalants. The preparation I prescribe is practically neutral, and the results in some cases are quite remarkable. . . .

p-Aminobenzoic Acid for Prurigo

Dr. DAVID S. CLARK (Yeovil, Som.) writes: I feel that the following case might be of some interest. I have a patient, a male aged 40, who has suffered every summer for the last eight or ten years from a form of prurigo aestivalis that has manifested itself as an itchy maculo-papular rash on any part of his body that has been exposed to the summer sun. The size and persistence of the spots vary with the intensity and length of the exposure, but half an hour's insolation has always been enough to produce the rash. By protecting the affected part from further sunlight and the use of local soothing remedies the rash has usually cleared in two or three weeks. On my advice he has been in the habit of avoiding sunlight as completely as possible, but at Easter this year his hands were exposed to the sun for over an hour. This provoked the usual rash. On this occasion I gave him no local treatment, but as a trial prescribed 200 mg. of *p*-aminobenzoic acid daily. For the first time in his memory the rash cleared within 48 hours. He has been taking this preparation regularly since and is now able to spend considerable periods in direct sunlight without suffering any ill effects.

Ante-partum Haemorrhage

Dr. TIM BOLAND (Sheffield) writes: In your report (April 17, p. 748) of the Edinburgh Obstetrical Society's meeting, Dr. R. de Soldenhoff advocated "the vaginal pack for certain emergency cases of ante-partum haemorrhage." Surely all obstetricians of repute are by now agreed that the vaginal pack has no place in the treatment of cases of ante-partum haemorrhage, whether emergencies or not. Any attempt to revive this shock-causing and septic procedure must be condemned.

Obituary

THE TRAGEDY OF MOUNT SCOPUS

We record with deep regret the deaths on April 13 of Dr. Doljansky, director of cancer research in the Hebrew University, Jerusalem; Dr. Yassky, director of the Hadassah medical service and deputy administrator of the cancer research department; Dr. Dostrovsky, physician at the University Hospital; Prof. Bonaventura, director of the psychology department; Dr. Ben-David, secretary of the medical faculty; and Mrs. Cassuto, assistant in the department of bacteriology. They were killed in an Arab attack on a convoy of the university staff, including doctors, nurses, and patients, travelling from the city of Jerusalem to Mount Scopus. Dr. Freiman, lecturer in Jewish law, Dr. Klar, lecturer in philology, and others in the convoy were also killed.

Prof. Enzo Joseph Bonaventura was born in 1891 at Pisa. He attended the University of Florence, took his doctorate in philosophy there, and then studied experimental psychology. In 1915 he was appointed assistant in the Institute of Psychology, and from 1923 to 1938 was professor of psychology. From 1924 to 1938 he was also professor of child psychology. In 1939 he was appointed professor of psychology at the Hebrew University, Jerusalem.

Dr. Leonid Doljansky was born at Ekaterinoslav, Russia, in 1898. He took his doctorate of medicine at Berlin University in 1925 and then did research at the Kaiser-Wilhelm Institute for Biology until 1928. From then until 1931 he conducted the Laboratory for Experimental Cytology at the Pasteur Institute, Paris. He then returned to Berlin University as an assistant in the Institute of Pathology. From 1933 until 1935 he carried out research at the Carlsberg Fondets Biologiske Institut at Copenhagen. In 1935 he was appointed head of the department of experimental pathology in the cancer research laboratories at the Hebrew University.

Dr. Aryeh Dostrovsky was born in 1887 at Cairo, in Russia, and attended the Universities of Vienna and Basle, taking his doctorate of medicine at Basle in 1915. He spent a year as house-physician at Basle University Children's Hospital and then went to Petrograd, as it was then called, to study skin and venereal diseases. From 1917 to 1918 he served as assistant at the skin hospitals of Dvinsk and Minsk, and from 1918 to 1920 as voluntary assistant at the Glavze Institute for skin and venereal diseases at Odessa. In 1920 he was appointed head of the department of skin and venereal diseases at the Rothschild Hadassah Hospital at Jerusalem, and in 1938 lecturer in dermatology and venereology in the Hebrew University.

Prof. Samson Wright contributes the following note: The Hebrew University and the University-Hadassah Hospital have suffered a grave blow as a result of many members of their staff having been killed by Arabs while going up in convoy to their place of work. I was invited two years ago by the University to go to Jerusalem to advise on the plans for the establishment of an undergraduate school of medicine. The University Hospital was completed just before the outbreak of war and is a fine, well-equipped building of some 400 beds doing first-class work. The Ratnoff Building alongside it houses the research and routine departments serving the hospital, such as those for pathology, biochemistry, hormone, and cancer research. Full facilities were thus available for the clinical part of the course. A good deal of postgraduate instruction in clinical and laboratory subjects was given during the war, and many R.A.M.C. officers enjoyed the facilities provided by the University for them. To complete the undergraduate school it was necessary to expand the existing departments of physics, chemistry, and biology, and to build new institutes for anatomy, physiology, and pharmacology. In addition the details of the course of instruction and examination had to be worked out.

During my stay in Jerusalem I came into intimate contact daily with most of the members of the staff, so many of whom are now dead. Yassky had long been the head of the Hadassah medical organization in Palestine and had been responsible for establishing throughout the country a network of hospitals, clinics, and specialist services of all kinds, which served faithfully not only the Jewish community but many Arabs also. Yassky had been the driving force responsible for building the Jerusalem Hospital, and he was chairman of the planning committee which was dealing with the medical school extensions. He was a man of great vigour of mind and body, and had an imagination restrained only by a keen sense of the practical. He is quite irreplaceable, for there is no one in Jerusalem with as complete a command as he had of the problems and their solution. The Biological Institute was started recently under his direction, and the building operations had continued in spite of the disturbances.

Dr. Ben-David, the secretary of the medical school, was a scholarly, patient, wise, and conscientious administrator who had made a special study of the problems of medical education and was particularly impressed with the Goodenough Report. He had to get agreement from a staff who had come from many lands and had brought with them their own university tradition, which each naturally wished the Hebrew University to follow. I had been in constant touch with him since my visit. His personality and knowledge will be sadly missed.

Dr. Doljansky was a first-class investigator in the field of cancer research and tissue culture. He belonged to the sensitive, artistic class of investigators. His laboratory was beautifully designed and arranged and appealed to the eye as well as to the mind. His technical skill was outstanding. His contributions to knowledge were numerous and distinguished. He had latterly acted as Dean of the Prefaculty of Medicine. With the death of Yassky, Ben-David, and Doljansky the medical school has simultaneously lost almost the whole of its leadership. I fear that the opening of the medical school to students, which had been planned for October of this year, will inevitably be delayed. No one knows what new disasters may yet befall Jerusalem in the coming months, but all friends of the Hebrew University will pray that it will survive to carry on its beneficent work for science and learning.

G. T. CALTHROP, M.D., D.M.R.E.

Dr. G. T. Calthrop died at his home at Luffenhall, near Stevenage, on April 14, at the age of 57. Gordon Thomas Calthrop was educated at Trent and Emmanuel College, Cambridge, graduating B.A. with honours in 1915. From there he went to the London Hospital, where he took the conjoint qualification in 1918, and the Cambridge M.B., B.Ch. the following year. After serving as house-physician at the London Hospital and as resident medical officer at the City of London Chest Hospital, during which time he took his D.P.H., Calthrop entered the service of the P. & O. as ship surgeon. His choice of a career was largely influenced by his physical disability, the result of a rheumatic carditis. It was at this time that Calthrop first became interested in radiology. He installed in his ship at his own expense a portable radiographic outfit. Possessed of a keen intellect, he found that his life at sea severely limited his activities, and in 1930 he decided to specialize in radiology.

Proceeding M.D. in 1930, Calthrop threw himself with zest into the study of radiology, and in 1932 he took the D.M.R.E. After a period in Germany under Albrecht and Berg, he started a private practice which increased at a remarkable rate on account of his superb technical skill and his high diagnostic ability. He rapidly gained hospital appointments, becoming radiologist to the Radium Institute, the Princess Beatrice Hospital, the Charterhouse Clinic for Rheumatism, and the Royal Free Hospital. Between his hospital work and his large private practice he undoubtedly overtaxed his limited physical capacity, and early in 1940 he was compelled to retire. To a person of Calthrop's temperament it was not easy to bow to the inevitable, and after a year's rest he came back to private and hospital practice against medical advice. To his friends, how he contrived to carry on until finally compelled to retire suddenly in 1946 will ever be a matter for amazement and admiration. Calthrop did not write much, but it was mainly due to his efforts that the Berg technique for the examination of the gastro-intestinal tract was introduced and popularized in this country. He is survived by a widow and a young son.

Dr. ARTHUR THOMAS TODD-WHITE died on March 14 at Woodford at the age of 78. The son of William White, historian, he was born at Sheffield in 1869. A student at Guy's Hospital, he qualified M.R.C.S., L.R.C.P. in 1893. He was clinical assistant at Guy's and later house-surgeon at the Lancaster Infirmary before taking up general practice in Lewisham and then in Leytonstone in 1898. While in practice he undertook the duties of clinical assistant at the Golden Square Hospital. He retired in 1946. The last of the old school in the area, he never really adjusted himself to this mechanical age, and he would dwell with obvious pleasure on the more leisurely and spacious days when, as a medical student, he voyaged to Australia in a sailing ship. He will be remembered for his many local activities. He was medical officer to the Post Office, divisional surgeon of the St. John Ambulance Brigade, and medical officer to the Clarnico Fire Brigade. In 1909 he established a scientific and military club for boys, and during the 1914–18 war he was one of the founders of the National Volunteer Reserve and later commanded the 3rd Essex Volunteer Battalion. For many years an active member of the British Medical Association, he was at one time honorary secretary and later chairman of the South-west Essex Division. In 1909 he published a paper in the *Guy's Hospital Gazette* advocating the appointment of a Minister of Public Health, and a later paper published in 1913 under the title "A National Medical Service" anticipated the National Health Service Act of 1946. Beloved by his patients, his wide interests in such varied subjects as geology, archaeology, ornithology, and philately assured him a wide circle of friends. He had outlived many who held him in high esteem, but to those that are left his death will be a sad loss. He leaves a widow, a daughter, and two sons. The daughter and the eldest son are members of the medical profession. The youngest son, Squadron-Leader R. N. Todd-White, was killed in 1943.

Dr. AILEEN MARION SETON POLLOCK, who died suddenly on March 29, had been a student at the London School of Medicine for Women and at St. Mary's Hospital. She qualified in 1927, and joined the staff of the Ludhiana Women's Christian Medical College in the Punjab two years later. On her first furlough in 1935 she took the F.R.C.S.Ed. By 1940 she had been appointed medical superintendent of the Ludhiana Hospital, and two years later she succeeded Dame Edith Brown as principal of the College. Dr. Pollock was well known in Scotland and in India for her work in connexion with medical education in the missionary field.

Dr. ARCHIBALD PATERSON ROBB died on April 3 after a short illness at the early age of 54. Born and educated in Glasgow, he qualified in 1918 in time to take a wartime commission in the Royal Navy. His bent was always towards psychiatry, and before entering general practice he was deputy superintendent at Gartloch Mental Hospital. In 1921 he settled in Edinburgh and carried on an ever increasing practice in the Merchiston district. For him, as for many others, the war years meant extra heavy burdens which he cheerfully undertook, adding to his other duties that of medical officer of a Home Guard battalion. There is little doubt that these hard years took their toll of his health, and some three years ago he had a warning that his strength was being unduly taxed. Some fifteen months ago he retired from practice, but still had sufficient vigour to continue his work on pension boards as consultant psychiatrist and on National Service boards. Dr. Robb had been a member of the B.M.A. since 1923, and was a representative at the Annual Representative Meeting in Dublin in 1933 and in London in 1935. He was chairman of the Edinburgh Division in 1945–6, and served on the I.A.S.C. (Scotland) 1933–4 and 1936–8, and also on the Public Medical Services Subcommittee 1936–7. He was medical secretary of the Edinburgh Panel Committee for ten years. He allowed himself little time for recreation, but the social side of life appealed to him, and whether as host or guest he was happy and anxious to share his happiness. He was able to enjoy only for a brief period his semi-retirement to the village of Duddington. He is survived by a widow and one son.—A. F. W. M.

Mr. HAROLD ROUND died on April 10 at his home in Edgbaston after a long illness. He was born in February, 1878, at Handsworth, and was educated at Aston Grammar School and Birmingham University, after being apprenticed to the late Mr. John Turner. He obtained the L.D.S. in 1900, the B.D.S. of Birmingham in 1901, and in 1902 was one of the first to be awarded the M.D.S. degree for his thesis on fractures of the jaw. He practised in Birmingham, and during the first world war, in collaboration with the late Prof. Billington and the late Mr. Arthur Parrott, was in charge of the jaw centre at the 1st Southern General Hospital. He held a similar post at Barnsley Hall, Bromsgrove, during the second world war. In 1919 he was appointed honorary dental surgeon to the Queen's Hospital, and when this amalgamated with the General Hospital to form the Birmingham United Hospital he transferred to the Queen Elizabeth Hospital. He was a past president of the Central Counties Branch of the British Dental Association and of the Odontological Section of the Royal Society of Medicine. He was the founder, and twice president, of the Odontological Section of the Birmingham Medical Institute. As recently as last year he became one of the foundation fellows in dental surgery of the Royal College of Surgeons. "H.R.," as he was known by his colleagues, was a man of strong principles and firm convictions. He was held in the greatest affection by his friends. He was conscientious to a fault, sparing neither his time nor his skill in the service of his many patients. The writer was closely associated with him for over forty years, and in common with all his colleagues held him in the highest esteem both as a man and an outstanding member of his profession. He was always unhurried, and nothing counted except the work in hand. Nothing would suffice but the very best. He has been known to give up a well-earned holiday because a dental colleague fractured his jaw and sought his aid—a kindliness that was only to be expected from him. Harold Round married Miss F. C. Tate, who died last year. Their only son, Dr. J. H. B. Round, died on active service in Palestine. He is survived by two daughters, to whom the greatest sympathy will be extended by his colleagues, patients, and many friends.—R. A. B.

Dr. Catherine Harrower writes: Through the death of Dr. Alison Mary Hunter a great and irreparable loss has been sustained, not only by the medical profession, but also by wide sections of the community which she served. Outside her professional duties she did much public work directed towards the welfare of women and children. As chairman of the National Vigilance Society she continued work in which her mother had already established a tradition. Throughout the months of her final illness Dr. Hunter never ceased to take a lively interest in the world outside her sick-room, and many were the personal and professional problems brought by her friends and colleagues for the sure illumination of her keen intellect. Alison Hunter will long be remembered by her many patients and friends for her loyalty, her compassion, and her unfailing readiness to put self aside in rendering help when called upon at any hour of day or night. She loved children and animals and all weak or suffering creatures, and her gallantry during a life of almost incessant hard work, followed by a long and trying illness, will remain an inspiration to all who knew her.

Medico-Legal

"ALKALOSIS" AND THE EFFECTS OF ALCOHOL

At Cambridge recently a defendant who was charged with driving a motor-car while under the influence of drink unsuccessfully pleaded illness as a defence in a case which occupied the court of Cambridgeshire Quarter Sessions, under the chairmanship of Mr. Gerald Howard, for two days—Jan. 30 and 31. The defendant admitted that he had taken some alcoholic drink on the evening in question, but he contended that it was quite insufficient, in a man of his constitution and habits, to affect his driving, and that his condition when arrested was due not to alcohol but to an excess of alkali which he had been taking for digestive trouble.

Dr. Alexander Brown, of Linton, who had been called in by the police to examine the defendant shortly after he was brought to the station, said that he came to the conclusion that the defendant was under the influence of drink. His speech was slurred, his gait unsteady, his pulse rate was 120, and his breath smelt strongly of alcohol. The Romberg test was positive. He was by turns truculent and jocose, and walked about the police station singing snatches of song. In cross-examination Dr. Brown said that he did not test his pupillary reaction, or his knee-jerks, or look at his tongue, or take a specimen of his urine. He was unaware that the defendant had had a duodenal ulcer or that some years ago he had undergone a short-circuiting operation. He had not complained of feeling unwell. The defending counsel asked whether Dr. Brown had considered that the defendant might be suffering not from alcoholism but from alkalosis.

Dr. Brown said that he had not had that condition specifically in mind, but he thought that for alkalosis to simulate alcoholism in its symptoms so large a quantity of alkali would have to be taken that almost no person could take it. He had never seen a case of alkalosis in general practice.

Dr. James Dundas Simpson, of Cambridge, who was called by the defence, said that his attendance had been requested by the defendant at the police station, where he arrived two hours after Dr. Brown had completed his examination. By then the defendant did not appear to be particularly the worse for drink, and the Romberg test was negative. Dr. Simpson's first impression was that drink was the only explanation of the defendant's conduct, and had he not subsequently obtained further information his conclusion would have been the same as Dr. Brown's. He learned later that this man, who had been a patient of his eighteen months previously for duodenal trouble, had been taking, not by his advice, large quantities of a proprietary alkali preparation. On the day of his arrest, according to his story, feeling unwell, he had consumed almost an entire bottle of this substance. His symptoms were consistent with alkalosis. Dr. Simpson had had one other case of alkalosis. This was a man on whom a gastro-enterostomy had been performed, and whose habit it had been for years to take large quantities of bicarbonate of soda. On one occasion he was picked up in a state of collapse, and proved to be quite uncoordinated; he staggered in his gait, was irrational in his speech, was incontinent, and showed such changes in his mentality that anyone observing him, and unaware of the facts, would have judged him to be a drunken man. Dr. Simpson did not suppose that any doctor in this country had any large experience of alkalosis, but it was a possible diagnosis which was tucked away in the mind. The cumulative effect of large quantities of soluble alkali absorbed into the blood stream might lead to a breakdown, either slow or sudden, liable to be precipitated by a chill or other factor. Chemical tests for alkalosis required very sensitive apparatus and were impracticable in an examination such as this at a police station. Many chronic dyspeptics, against their doctor's advice and without his knowledge, consumed much-advertised preparations in order to obtain relief from intestinal pain and discomfort, and the danger of poisoning by alkalis was not to be disregarded.

After a long hearing the jury returned a verdict of guilty on the main charge, and the accused was fined £50. On a second charge, that of driving a motor-car in a manner dangerous to the public, he was also found guilty and fined £1. He was disqualified from holding a driving licence for one year.

Appeal Dismissed

The defendant's appeal against his conviction was heard on April 19. The substantial ground of the appeal was that the evidence given by Dr. Alexander Brown, who was called in by the police, was inadmissible.[1] Mr. Justice Humphreys, giving the judgment of the Court, said that the appellant had been seen driving on the wrong side of the road and without lights, and that on examination by the police he appeared to be drunk. They took him to a police station, and there the ordinary procedure was carried out. Following an order circulated to police stations years ago a police doctor was sent for. This doctor told the appellant that he could have his own doctor. The appellant said that he had never had a doctor in his life. The police doctor then examined the appellant and certified him to be in an alcoholic state and unfit to drive. This evidence was said to be inadmissible. The appellant had not wished to be examined, but kept singing and was awkward. The doctor had eventually persuaded him, saying that an examination might be to his advantage. The doctor had behaved perfectly reasonably. The law which excluded evidence of a confession extracted by means of a promise or a threat had nothing to do with this case and the appeal would be dismissed.

Counsel for the appellant had referred to the recent Scottish case of *Reed* v. *Nixon* (1948) in which the conviction in a similar case had been quashed. The Lord Advocate had then conceded that in all such cases the police doctor was acting as "the hand of the police." Mr. Justice Humphreys mentioned this point. Their lordships did not agree that that was true in England. The evidence of a police doctor should be accepted in the same way as the evidence of any other professional man. It must be presumed that he came before the Court with the desire to assist it and with no other desire.

[1] *The Times*, April 20.

Universities and Colleges

UNIVERSITY OF LONDON

The Academic Postgraduate Certificate in Public Health has been awarded to D. Coueslant, T. H. Elias, W. K. Laing, and D. N. Phukan, all of the London School of Hygiene and Tropical Medicine.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

The otolaryngology lecture course which was to have been held at the College from April 26 to May 12, has been cancelled.

SOCIETY OF APOTHECARIES OF LONDON

Prof. E. C. Dodds, F.R.S., Master, presided at a recent meeting of the Court of Assistants, when the resignation of Dr. Cyril H. T. Ilott was received with great regret.

The Court considered the present position with regard to the National Health Service and it was resolved to forward a resolution to the British Medical Association expressing the hope that further negotiation between the Minister of Health and the profession would be made possible.

The following were appointed as representatives of the Society: Dr. J. Prescott Hedley, on the Central Midwives Board, and Dr. Frank Howitt at the International Congress on Physical Education, Recreation, and Rehabilitation.

The Gillson Scholarship in Pathology was awarded to Alan C. Thackray, M.D.

It was announced that on July 7 the Society's gold medal in therapeutics will be presented to Sir Lionel Whitby, M.D., F.R.C.P., Regius Professor of Physic in the University of Cambridge.

Authority was given for the Society's Coat of Arms to be incorporated in a memorial window at Westminster Hospital to the late Sir Stanley Woodwark.

Sir Frederick Michael Wells, Lord Mayor of London, was admitted to the Freedom of the Society, the first occasion, it is believed, on which the Lord Mayor of London has been admitted to the Freedom of a City Company during his year of office.

It was resolved that a course of ten lectures on modern therapeutics be delivered in the Great Hall in the autumn.

The Diploma in Industrial Health was granted to A. M. Critchley, D. Fowler, V. O. B. Gartside, A. French, R. Swinburn, and S. A. Underwood.

The Diploma of L.M.S.S.A. was granted to E. F. Jones, L. T. Al-Badri, M. K. A. El Banhawy, C. F. M. Fisher, W. L. M. Garsia, D. J. Sheerboom, I. F. Dajani, S. K. A. D. J. Bernhardt, E. L. Gilbert, C. K. Cumming, P. C. J. Nicholl, C. H. J. Van Aswegen, M. P. Coplans, and M. J. Bhavnani.

Medical Notes in Parliament

Manor House Hospital

On April 22 Mr. GAMMANS inquired for what reason the Manor House Hospital and the Manor House Clinic, Hampstead, were to be exempted from the National Health Service.

Mr. BEVAN replied that it appeared to him that their transfer was not required for the purpose of providing hospital and specialist services under the Act.

Imported Books

Mr. SWINGLER on April 22 invited the President of the Board of Trade to make a further statement about imports of learned, scientific, and technical books.

Mr. HAROLD WILSON replied that he had been going into this question. He had always been aware of the strength of the case for increasing imports of the classes of books mentioned, although he had to balance this against the exchange position. He was now able to tell the House that learned, scientific, and technical books could, as from April 1, be imported at twice the present rate, thus raising the annual import quota to 200% by value of the pre-war level.

(The need for this increase in the quota allowed to importers was discussed in a leading article in our last issue—p. 793.)

Criminal Justice Bill

On April 15, during the report stage of the Criminal Justice Bill, Mr. EDE moved to amend Clause 6 by adding words to ensure that refusal to undergo surgical, electrical, or other treatment should not be regarded as a breach of a probation order if, in the opinion of the court, the refusal was reasonable having regard to all the circumstances. He said it had not been found possible to draft the amendment so as to provide that refusal to undergo a surgical operation should not be regarded as a breach of a probation order relating to mental treatment. The term "surgical operation" would apparently include an injection or electrical treatment. The amendment was agreed to.

Ice-cream.—Mr. BEVAN told Mr. GEOFFREY COOPER on April 22 that he was not prepared to introduce a licensing scheme or a scheme for the grading of ice-cream as a public safeguard to ensure easily recognized standards of cleanliness in the preparation and the food content. Mr. Bevan added that a high degree of cleanliness was obtainable under existing Acts and Regulations.

Hadassah Hospital.—Dr. SEGAL inquired on April 21 whether the responsibility of the Government of Palestine for the maintenance of law and order until May 15 included the safeguarding of free access of medical and nursing staffs to their hospitals; and whether the Hadassah Hospital in Jerusalem was included under these arrangements. Mr. MAYHEW replied that free access of medical and nursing staffs to their hospitals was being safeguarded so far as resources permitted. Comparative freedom of travel on the road which led from the City of Jerusalem through an Arab quarter to the Hadassah Hospital had been maintained for some weeks by military action but was interrupted on April 13 by an attack launched by Arabs on a convoy, apparently in retaliation for the murder of Arabs by Jews at Deir Yassin. It was understood that in view of this incident the Jewish authorities decided to evacuate the Hadassah Hospital.

Last Panel Cheques.—Mr. BEVAN, in reply on April 22 to Sir ERNEST GRAHAM-LITTLE, said that the payments an insurance doctor would receive for the period Jan. 1 to July 4, 1948, would be based on the average of the number of persons on his list on Jan. 1 and April 1.

EPIDEMIOLOGICAL NOTES

Discussion of Table

In *England and Wales* an increased incidence was recorded for whooping-cough 664 and measles 319. There was a decreased incidence for scarlet fever 225, acute pneumonia 61, and dysentery 77.

A rise in the number of notifications of whooping-cough was recorded in most areas of the country; the largest rises were Essex 102, Yorkshire West Riding 101, Middlesex 73, and Lancashire 58. Considerable variations occurred in the local trends of measles. The largest increases were Surrey 279, Lancashire 204, and London 90; the largest decreases were Hertfordshire 122, Northamptonshire 117, Norfolk 94, and Middlesex 82. With the exception of a decrease of 67 in Lancashire there were no large changes in the local trends of scarlet fever. No changes of any size were reported in the returns for diphtheria.

The chief centres of dysentery were Lancashire 41, London 18, and Yorkshire West Riding 17. Durham with 2 cases of poliomyelitis was the only county with more than 1 notification.

In *Scotland* increases occurred in the notifications of measles 150, whooping-cough 23, and dysentery 12, while there were decreases in the incidence of scarlet fever 67, acute primary pneumonia 37, and cerebrospinal fever 16. An outbreak of diphtheria involving 11 persons was notified in Dumbarton county. The largest returns for dysentery were Paisley 16 and Edinburgh 12.

In *Eire* there were increases in the incidence of measles 40 and primary pneumonia 17. Falls were recorded in the notifications of scarlet fever 18 and whooping-cough 17. The increased incidence of measles was largely contributed by Dublin C.B. The fall in the notification of scarlet fever was mainly confined to the country districts.

In *Northern Ireland* increases were reported in the notifications of diphtheria 9 and whooping-cough 11, while a decrease of 9 was recorded for scarlet fever and for measles. Measles and whooping-cough reflect the trends of these diseases in Belfast C.B., while the changes in the incidence of diphtheria and scarlet fever were due to the experience of the country areas.

Week Ending April 17

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,290, whooping-cough 3,888, diphtheria 136, measles 9,681, acute pneumonia 639, cerebrospinal fever 47, acute poliomyelitis 19, dysentery 110, paratyphoid 7, and typhoid 9.

No. 15

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended April 10.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.
Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for: (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.
A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

Disease	1948 (a)	(b)	(c)	(d)	(e)	1947 (Corresponding Week) (a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	36	2	19	6	—	89	7	36	—	1
Deaths		—	—				—	1		
Diphtheria	155	15	48	14	10	213	18	55	18	5
Deaths	4	—	—	—	—	1	—	—	—	1
Dysentery	111	18	50	—	—	77	6	11	—	1
Deaths				—	—				—	—
Encephalitis lethargica, acute	—	—	1	—	—	—	—	—	—	—
Deaths		1					—			
Erysipelas			43	7	8			49	11	2
Deaths		—					—			
Infective enteritis or diarrhoea under 2 years				30					38	
Deaths	48	5	6	1	1	85	14	18	7	—
Measles*	11,193	1809	445	130	44	10,326	525	223	36	26
Deaths†			2	1	—	12	1	1	1	1
Ophthalmia neonatorum	65	7	16	—	—	61	6	22	—	—
Deaths										
Paratyphoid fever	3	—	1 (B)	2 (B)	—	1	1	—	—	—
Deaths	—	—	—	—	—	—	—	—	—	—
Pneumonia, influenzal	703	45	6	11	1	709	38	14	9	11
Deaths (from influenza)‡	9	—	1	1	—	33	7	4	—	2
Pneumonia, primary			226	44				238	33	
Deaths	207	35		10	11		52		13	12
Polio-encephalitis, acute	2	—				—	—			
Deaths							—			
Poliomyelitis, acute	14	—	3	1	—	11	4	—	—	—
Deaths§	2	—					—			
Puerperal fever		1	9		—		3	15		—
Deaths										
Puerperal pyrexia‖	135	8	8	—	—	156	12	10	1	1
Deaths		—					—			
Relapsing fever	—	—			—	—	—			—
Deaths										
Scarlet fever	1,196	79	238	28	34	928	73	177	18	25
Deaths†			—	—	—	—	—	—	—	—
Smallpox	—	—	—	—	—	13	—	—	—	—
Deaths				—	—				—	—
Typhoid fever	7	1	—	—	—	6	—	—	7	1
Deaths	—	—	—	—	—	—	—	—	—	—
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths				—	—				—	—
Whooping-cough*	3,303	231	45	35	24	1,751	221	146	104	7
Deaths	14	2	1	—	1	26	4	2	8	—
Deaths (0–1 year)	349	45	46	23	12	555	68	97	37	16
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	4,853	741	589	189	130	5,469	883	722	254	151
Annual death rate (per 1,000 persons living)			11·9	11·8				15·0	16·3	
Live births	8,752	1460	1020	482	293	10,291	1664	1336	477	287
Annual rate per 1,000 persons living			20·6	30·2				26·9	30·6	
Stillbirths	226	30	38			246	35	48		
Rate per 1,000 total births (including stillborn)			36					35		

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.
† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.
‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.
§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.
‖ Includes puerperal fever for England and Wales and Eire.

Medical News

Papers for the Cambridge Meeting

Those reading Opening Papers in the Scientific Sections of the B.M.A. Annual Meeting at Cambridge in June are reminded that their papers, with full summaries, should have been in the hands of the Editor of the *British Medical Journal* on May 1, so that arrangements can be made for the printing of the summaries. Will those who have not yet sent in their papers kindly do so at the earliest opportunity.

Government Reception

The Government held a reception on April 21 at the General Register Office, Somerset House, in honour of the members of the Canadian and United States Delegations concerned with Medical Nomenclature and Statistics. Mr. Aneurin Bevan, the Minister of Health, and Mrs. Bevan received the guests.

Society of Chiropodists

The Society of Chiropodists held a successful Annual Convention in London on April 22, 23, and 24. At a dinner at the Savoy Hotel on Friday, April 23, the many guests were received by the President, Mr. John H. Hanby, who is instructor in chiropody at Guy's Hospital. Sir Heneage Ogilvie proposed the toast of the Society and described the cordial relations between the Society and the Royal College of Surgeons. In his reply Mr. Hanby referred to the importance of chiropody in connexion with the care of school children and in industry. Mr. Charles Challen, M.P., proposed the toast of the medical profession and Sir Alfred Webb-Johnson, P.R.C.S., replied.

Hogarth Centre

The radiotherapeutic centre at the Nottingham General Hospital has been renamed the Hogarth Centre in recognition of the outstanding services of Mr. R. G. Hogarth, who has attained his 80th birthday, in treating cancer. The announcement was made by the Duke of Portland at the annual meeting of the Notts Council of the British Empire Cancer Campaign recently.

Gift to Royal College of Physicians

The British Red Cross and St. John War Organization has given £20,000 to the Royal College of Physicians in recognition of the services rendered it by the medical profession during the war. It will be used to develop the library, particularly to help students of the history of medicine.

New Journal of Plastic Surgery

The first number of the *British Journal of Plastic Surgery* has been published by the British Association of Plastic Surgeons under the editorship of Mr. A. B. Wallace, of Edinburgh University. It is particularly well produced, the illustrations being remarkably clear. This number contains articles on "Plastic Surgery in the Training of Surgeons," by Mr. Paterson Ross, "Congenital Absence of the Penis," by Sir Harold Gillies, "Deformities of the Male Urethra," by Sir Archibald McIndoe, and other papers by Mr. Rainsford Mowlem, Mr. James B. Cuthbert, Mr. F. T. Moore, and Mr. M. C. Oldfield.

Dentists Request Interview with Minister

The Dental Consultative Committee has asked the Minister of Health for an interview, and also that he consider incorporating amendments in the N.H.S. Act. It requests an Amending Bill to prevent the formation of a whole-time salaried service by Regulation as well as other possible amendments.

National Insurance

After July 5 those medical practitioners on the lists of Executive Councils under the N.H.S. Acts will be classed as self-employed persons for the purposes of paying insurance contributions under the National Insurance Act, 1946 (Preliminary Draft of the National Insurance (Classification) Regulations, 1948).

History of Medicine

At the inaugural meeting of the Scottish Society of the History of Medicine, held on April 23 in the hall of the Royal College of Surgeons of Edinburgh, Dr. H. J. C. Gibson read a paper on "The Early Days of the Dundee Royal Infirmary," of which institution he is medical superintendent. He said that the Infirmary originated in a dispensary which was founded in 1735 and reorganized in 1782 by the minister of the parish. He was assisted in his philanthropic effort by Mr. Stewart, surgeon, and by Sir Alexander Douglas, Bt., physician, members of the medical staff when the first patient was admitted to the Infirmary in 1798. The cost of the original building was £1,400, and £40 was allotted for the purchase of surgical instruments. The sick and injured "whose home conditions were deficient" came at 11 o'clock each Thursday, unless they travelled from a distance or had met with dangerous accidents, when they were admitted at any time. The decision on eligibility for admission rested with the Weekly Board. A maintenance charge of 3s. 6d. per week was payable by the Governor who had recommended the patient. Dr. Gibson traced the history of the hospital from those early days to the building of the new Infirmary in 1855, by which time it had become, as it still remains, one of the chief voluntary hospitals of Scotland, serving the needs of patients from Angus, East Fife, and Perthshire.

At the close of his address the speaker was thanked by Dr. W. D. D. Small, President of the Royal College of Physicians of Edinburgh.

Dr. Douglas Guthrie, who has been elected President of the Society, explained that it was founded to create and extend interest in the history of medicine throughout Scotland. The Hon. Secretary, Dr. H. P. Tait, 137, Colinton Road, Edinburgh, will be glad to hear from any who are interested. At the second meeting, to be held in June, Dr. John Ritchie will address the Society on "Quarantine for Plague in the Sixteenth and Seventeenth Centuries."

COMING EVENTS

"Darkness into Daylight"

An exhibition to mark 100 years of research and achievement in electric lighting, entitled "Darkness into Daylight," opens to-day (Friday, April 30), at 10 a.m., at the Science Museum, South Kensington, London, S.W., and will remain open until the end of September. The hours of admission are 10 a.m. to 6 p.m. on weekdays and 2.30 p.m. to 6 p.m. on Sundays.

Westminster Hospital Ladies' Association

The annual meeting of the Westminster Hospital Ladies' Association will be held in the Queen Mary Nurses' Home of the hospital (entrance in Page Street), on Wednesday, May 5, at 3 p.m., when Emeritus Prof. Winifred Cullis will give an address and the house-governor will speak on "The Future Outlook."

Centenary of First Public Health Act

The Corporation of London has arranged a dinner to be held in the Guildhall Library on Friday, May 7, at 6.45 p.m. for 7.15 p.m., to commemorate the centenary of the first Public Health Act.

French Refresher Course

A course devoted to recent advances in medicine will be held on May 21 to 23 at the Clinique Propédeutique of the Broussais Hospital, 96, Rue Didot, Paris. Further information may be obtained from Prof. Jean Hamburger, 29, Boulevard de Courcelles, Paris, VIIIe.

Physical Medicine

The British Association of Physical Medicine announces that its Belgian counterpart, La Société Belge de Physiothérapie, has arranged for an International Meeting of Medical Electronics to be held in conjunction with the Journées Médicales in Brussels from June 13 to 16. The object of the meeting is to bring together medical men and physicists and enable them to exchange views on subjects within the following fields: (1) General physics in relation to its application to medicine; (2) photo-biological and electro-biological principles of direct importance to medicine; (3) medical electrology with special reference to diagnosis and treatment; (4) equipment and dosimetry. Those wishing to attend or to make scientific contributions are asked to communicate with Dr. L. Konings, Rue Vilain XIV, 43, Bruxelles, Belgium.

SOCIETIES AND LECTURES

Monday

EDINBURGH UNIVERSITY: PHYSIOLOGY CLASSROOM.—May 3, 5 p.m. "*Medicine and Philosophy*," by Dr. Douglas Guthrie.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—May 3, 2.30 p.m. "*Facial Paralysis. Bell's and other Palsies. Nerve Grafts. Nerve Anastomosis*," by Miss D. J. Collier.

LIVERPOOL PSYCHIATRIC CLINIC.—At Town Hall, Liverpool, May 3, 3 p.m. Annual meeting. "*New Pathways in Psychiatry*," by Prof. H. V. Dicks, M.D., M.R.C.P.

WESTMINSTER HOSPITAL SCHOOL OF MEDICINE: MEYERSTEIN LECTURE THEATRE, Horseferry Road, S.W.—May 3, 5.30 p.m. Clinico-pathological demonstration. Discussion: "*Emphysema*."

Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Edinburgh Royal Infirmary, May 4, 5 p.m. "*Salt and Water Parallelism*," by Prof. Kerpel-Fronius.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—May 4, 5 p.m. "*Dermatophytes*," by Dr. I. Muende.

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATION.—At B.M.A. House, Tavistock Square, London, W.C., May 4, 8.30 p.m. Social meeting.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHYSIOLOGY.—At Physiology Theatre, Gower Street, London, W.C., May 4, 5 p.m. "*The Physiological Aspect of Speech*," by Mr. D. B. Fry, Ph.D.

Wednesday

GLASGOW UNIVERSITY: DEPARTMENT OF OPHTHALMOLOGY.—May 5, 8 p.m. *"The Growth of Ocular Vessels,"* by Dr. I. C. Michaelson.

ROYAL SOCIETY OF ARTS, John Adam Street, Adelphi, London, W.C.—May 5, 2.30 p.m. Pope Memorial Lecture: *"Recent Advances in Stereochemistry,"* by Mr. F. G. Mann, D.Sc., F.R.S.

Thursday

EDINBURGH ROYAL INFIRMARY.—May 6, 4.30 p.m. Honyman Gillespie Lecture: *"The Experimental and Clinical Use of Anti-Histamine Drugs,"* by Dr. R. B. Hunter.

FACULTY OF HOMOEOPATHY.—At London Homoeopathic Hospital, Great Ormond Street, London, W.C., May 6, 5 p.m. *"The Evolution of Clinical Pathology,"* by Dr. William Briggs.

INSTITUTE OF DERMATOLOGY, 5, Lisle Street, Leicester Square, London, W.C.—May 6, 5 p.m. *"The Seborrhoeic Eruptions,"* by Dr. B. Russell.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—May 6, 3 p.m. *"A Modification of Laryngectomy,"* by Dr. Jean Leroux-Robert (Paris). Illustrated by a cinematograph film. 5.30 p.m. *"Diseases of the Antrum of Dental Origin,"* by Mr. J. Angell James.

LONDON JEWISH HOSPITAL MEDICAL SOCIETY.—At London Jewish Hospital, Stepney Green, E., May 6, 3 p.m. *"Medical Statistics,"* by Dr. J. Bronowski.

ROYAL PHOTOGRAPHIC SOCIETY.—At 16, Prince's Gate, London, S.W. May 6, 7 p.m. *"Photomicrography."* Lecture by Mr. F. J. Pittock, F.R.P.S.

Saturday

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, London, W.C.—May 8, 11 a.m. *"Modern Temporal Bone Surgery. The Philosophy of Its Evolution,"* by Dr. Julius Lempert (New York).

APPOINTMENTS

Percival V. Pritchard, M.D., F.R.C.P.Ed., F.R.F.P.S., has been appointed to the Northern Ireland General Health Services Board.

CHRISTIE, THOMAS, M.D., Medical Officer, H.M. Prison, Holloway.

MARTIN, K. W., M.B., B.S., F.R.C.S., Resident Surgical Officer and Surgical Registrar, Worthing Hospital.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Bard.—On April 14, 1948, at Queen Mary Hospital, Hong Kong, to Sophie Bard, M.R.C.S., L.R.C.P., wife of Dr. S. M. Bard, a daughter.

Brewerton.—On April 5, 1948, at 9, Lancaster Grove, London, N.W., to Sylvia, wife of Dr. R. Brewerton, a daughter—Jane Elizabeth.

Nelson.—On April 15, 1948, at Salisbury General Infirmary, to Albertine (née Van Calck), wife of Maurice P. Nelson, M.R.C.S., L.R.C.P., a son—Robert François.

Williams.—On April 20, 1948, at Queensgate Clinic, London, S.W., to Lois Carol (née Schear), formerly of Evansville, Indiana, wife of Dr. A. H. Williams, a son—Stephen Joseph.

DEATHS

Brunlees.—On April 18, 1948, Oswald Brunlees, L.R.C.P.&S.Ed., L.R.F.P.S. Glas., of 75, Denmark Villas, Hove, Sussex, aged 68.

Clarke.—On April 18, 1948, at 2, Wood Villas, Clifton Road, Prestwich, Lancs, Maude Patricia Smart Clarke, M.B., B.Ch.

Cuthbert.—On April 24, 1948, at Hindhead, Surrey, Margaret Jane Mudie Cuthbert, M.B., Ch.B.

Fleming.—On April 10, 1948, Thomas Loudon Fleming, M.B., Ch.B., aged 60.

Forge.—On April 19, 1948, at Boscombe Hospital, George Baynton Forge, M.R.C.S., L.R.C.P., of Handley, Dorset, aged 76.

Gardiner.—Recently, John Percival Gardiner, M.B., Ch.B.Ed., of Pendeen, near Penzance, Cornwall.

Gilchrist.—On April 15, 1948, Norman William Gilchrist, M.B., Ch.B., of The Hall, Bloxwich, Staffs.

Glass.—On April 21, 1948, at The Shelling, Grantown-on-Spey, Alexander Gibb Glass, M.D.Ed., formerly M.O.H., Farnworth, and late of Bolton, Lancs.

Goddard.—On April 20, 1948, Gerald Hamilton Goddard, D.S.O., M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C.

Grapel.—On April 20, 1948, Francis Gaspar Grapel, M.R.C.S., L.R.C.P.

Guttmann.—On April 25, 1948, Eric Guttmann, L.R.C.P.&S.Ed., L.R.F.P.S. Glas., of Maudsley Hospital, London, S.E., aged 52.

Hill.—On April 14, 1948, at 21, Magdala Road, Nottingham, Philip Keith Hill, M.R.C.S., L.R.C.P., aged 65.

Lidderdale.—On April 20, 1948, at Cheltenham General Hospital, William Guy Lidderdale, M.B., B.S., of Shillington, Hitchin, Herts.

Martin.—On April 19, 1948, at Hove, Mary Edith Martin, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., aged 72.

Newport.—On April 19, 1948, Alexander Charles William Newport, C.V.O., M.R.C.S., L.R.C.P., Surgeon Captain, R.N. retired, of 17, Cousins Grove, Southsea.

Temple.—On April 19, 1948, at Knockdolian, Comrie, Perthshire, Charles Dunbar Temple, M.B., C.M.Glas., aged 85.

Thomson.—On April 16, 1948, at Derbyshire Royal Infirmary, George Thomson, M.B., C.M.

Williams-Walker.—On April 22, 1948, at 86, Anderton Park Road, Moseley, Alfred Williams-Walker, M.D., M.R.C.P.

Wrigley.—On April 26, 1948, at a Huddersfield Hospital, Kenneth Graham Wrigley, L.M.S.S.A., aged 53.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Normal Blood-pressure Readings

Q.—*What do you consider to be the normal systolic/diastolic readings for adults under 50, aged 50 to 65, and over 65 years of age? It appears to me that, according to the tables of insurance companies, the majority of patients over 50 have hypertension. Textbooks advise prohibition of alcohol and drastic reduction in salt for patients suffering from arteriosclerosis or hypertension. Is there anything to be gained by compelling patients over 65, with hardening of arteries and/or some rise in blood pressure, to forgo the pleasure of using salt and alcohol as their inclination suggests? Is there not some risk in depriving patients of salt over a long period?*

A.—This reply deals not with casual but with basal readings—i.e., those found at repeated examinations under resting conditions. The upper limits of normal pressure for adults at various ages are: below 50, 150/90 mm. Hg; between 50 and 65, 155/95 mm. Hg; and over 65, 160/95 mm. Hg. Pressures above the last figure represent hypertension at any age, although slight excesses are of less and less significance in later ages. For life assurance examinations the blood pressure is best registered after a few minutes' recumbency, the lowest of two or three recordings being taken. The type of case described in the last half of the question does not require prohibition of alcohol or drastic salt restriction, although both articles should be kept well within moderate limits. The degree of salt restriction obtainable by avoidance of salt in cooking and at table is without risk even over a long period.

Animal Ringworm in Farm Workers

Q.—*Recently I have had several cases of animal ringworm in farm workers. Is there more than one kind of animal ringworm, and does it affect all persons in the same way, as the lesions appear to differ? Liquor iodi fortis, ung. hydrarg. ammon. co., and ung. iodi B.P. have all been tried without much success. Is treatment by x rays of any value?*

A.—Animal ringworm may be of many types, both small-spore and large-spore, but most of the cattle ringworm infections are of the large-spore ectothrix variety. The small-spore varieties produce very little more inflammation on the skin than does the ordinary human small-spore infection, but large-spore infections produce varying degrees of inflammatory reaction, with redness, vesication, and pustulation right up to the type of lesion described as kerion, with great swelling, oedema, and congestion, and a follicular pustular reaction over the area involved. The fierce reaction is a natural response to the foreign invasion, and is part of the mechanism of cure. The introduction of local treatment will sometimes precipitate such a pustular reaction. The most effective local applications are ung. dithranol B.P. and the following paint, fomentations often being necessary:

℞

Hyd. perchlor.	½%
Brilliant Green	½%
Spirit	ad 100%

Make a paint.

X rays are of no value in the treatment of ringworm infections in these cases.

Discoloration of Adrenaline Solutions

Q.—*What changes cause the discoloration of solutions containing adrenaline? How do these changes affect the physiological action of the drug? Should the solution be acid to prevent discoloration? What substances are used to prevent deterioration?*

A.—The darkening in colour of a solution of adrenaline is caused by the gradual decomposition of the adrenaline hydro-

chloride in it; this naturally reduces the activity of the solution, and it eventually becomes inert. It is necessary to have the solution slightly acid, in the first place because adrenaline itself is only very sparingly soluble in water and must be converted to the hydrochloride or another salt, and secondly because it is more stable in somewhat acid solution. Various substances may be used to prevent or retard the decomposition of adrenaline. Sodium metabisulphite in a concentration of 1 in 1,000 is the chemical favoured at present, but other antoxidants are useful, and glycine in a concentration of 1 in 500 is also effective.

Thorotrast and Sarcoma Formation

Q.—*Is there any evidence that the intravenous injection of "thorotrast" may lead to sarcoma formation at a later date?*

A.—Yes. Several authors, including G. Roussy, C. Oberling, and M. Guérin (*Bull. Acad. Méd., Paris,* 1934, **112**, 809), have shown that the injection of thorium dioxide may produce sarcomata in experimental animals, and especially in the rat. More recently H. E. MacMahon, A. S. Murphy, and M. I. Bates (*Amer. J. Path.*, 1947, **23**, 585) have provided evidence which, although derived from a single case, nevertheless indicates that thorotrast may also act as a sarcogenic agent in man. The patient had been given thorotrast intravenously for visualization of the liver, and by this means it was possible to make an accurate diagnosis of hepatic syphilis with gumma. Following specific therapy the patient made a clinical recovery. After sudden death twelve years later, necropsy confirmed the diagnosis of syphilis and in addition revealed fatal haemorrhage from a sarcoma of the liver, with widespread irradiation injury chiefly affecting the liver and the haemopoietic system.

Introduction of Cholera into Egypt

Q.—*How did cholera get to Egypt last September?*

A.—Despite the fullest inquiry and investigation by the Egyptian Government the source and mode of introduction of cholera into Egypt last September were not discovered. It seemed likely that infection had been occurring before the first cases were recognized in an Egyptian village on Sept. 22, 1947. The infection presumably came from one of the endemic regions in India, from which in the past there were three possible routes to Egypt: (1) the long land route through Afghanistan and Iran—nowadays most unlikely; (2) by the Persian Gulf to Irak and on to Syria and the Mediterranean; (3) by the Red Sea direct to Egypt. To these must nowadays be added the air routes from India via Egypt and Arabia. In spite of rumours and allegations there was no evidence to suggest that the Royal Air Force or the British Army was responsible for last year's introduction of cholera into Egypt.

Antrochoanal Polypi

Q.—*Are antrochoanal polypi usually associated with anosmia? In a case in which the antra have been cleared the anosmia persists. What treatment is advised?*

A.—Antrochoanal polypi are not, as a rule, associated with anosmia. They are almost invariably unilateral, and to cause anosmia mechanically must be large enough to block both choanae completely. If the ethmoids are clear probably no further treatment will help.

Renal Rickets

Q.—*A woman 28 years old suffered from rickets at the age of 1½ years, and is now a typical "rickety dwarf." At her age is there any possible hope of straightening the bones of the legs by operation?*

A.—If this patient is suffering from ordinary rickets due to lack of vitamin D there is no reason at all why the legs should not be straightened by osteotomies. The age of onset, however, and the fact that she is a dwarf strongly suggest that she may have "renal rickets." In these patients kidney function is so poor that an anaesthetic or an operation will often precipitate a fatal uraemia. Therefore, before any decision is made for or against operation, renal function should be thoroughly tested.

Penicillin for Actinomycosis

Q.—*What is the recommended dose of penicillin for actinomycosis?*

A.—The dose of penicillin should be large and should be continued for a long time: 250,000 units every six hours or 500,000 twice in the 24 hours would be about the dose necessary for a severe infection of thorax or abdomen. Half that dose would probably suffice for a face or neck infection. The drug must be administered for a month or two continuously. When given in concentrated form the injections are not too painful, but procaine hydrochloride should be put in the syringe in order to diminish the discomfort.

NOTES AND COMMENTS

Liquid Paraffin for Cooking.—Mr. P. ROCHE, Editor of *The Retail Chemist*, writes: Although the answer to the inquiry made under this heading (April 17, p. 769) recommends that "its use [liquid paraffin] as a substitute for vegetable oils in salad creams and cooked products generally should be prohibited by law," it does not indicate that there is still in operation a Government Order which deals with this very point. I refer to the Control of Petroleum Order, 1944, S.R. & O. 1944, No. 171, which says in effect that no person shall use any liquid paraffin (B.P.), except for medicinal purposes, except when having a licence to do so. Obviously any general member of the public using this substance for the purposes you mention is breaking the law, and, although one can assume that it has been contravened time and time again, I doubt whether an offender has yet been charged, although the Order has been in force now for over four years. This seems to be another instance where the multiplicity of Orders precludes their being effectively enforced, presumably because of the lack of inspectors. Even if there were sufficient, which heaven forbid, it would not be easy to see that every housewife used liquid paraffin for medicinal purposes only, particularly when she can buy it with no questions asked. The matter takes on another serious aspect when supplies have reached the fixed price stores and yet the dispensing chemist has not been able to obtain sufficient to meet prescription requirements. Would it not be better, therefore, if the channel of distribution is limited to that of the chemist, who can at least obtain a verbal acknowledgment that the liquid paraffin he sells is going to be used for "medicinal purposes" only?

Killing Habits of Leopards.—A correspondent in W. Africa writes: Under "Any Questions?" (March 13, p. 530) you answer a question about leopards. I think I can help in answer to (*d*). Some years ago a woman was brought into hospital with a cut head. On inquiry I found that a leopard had jumped at her and had given her one blow with its paw—claws extended. She had a small puncture just above the middle of one clavicle, a clean cut through the ear and right across the scalp to the other ear, and two quite clean cuts parallel to this one and about two inches in front and behind it. They were about four or five inches long. As far as I could make out the puncture in the neck was made by the fifth claw, the main cut by the middle claw, and the other two by the index and ring fingers (if leopards have such things). The woman was almost scalped, and was shocked. She had not lost much blood. Cleaning with flavine and suturing were followed by rapid healing. It appeared that the leopard had been disturbed by the woman and had given her a pat in self-defence. There was no suggestion of "leopard men" in that area. The cuts were very clean.

Corrections

The name of the Medical Director of the Empire Medical Advisory Bureau was misspelt in our issue of April 24 (p. 809). It should be Dr. H. A. Sandiford.

In the letter by Dr. I. H. Milner (April 24, p. 807, line 10) the word "complicated" should be "uncomplicated."

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